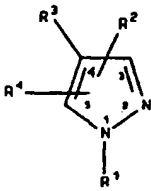




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

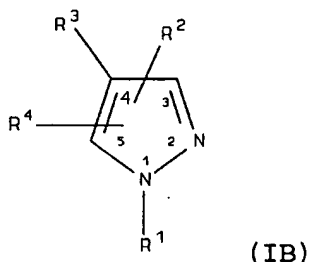
<p>(51) International Patent Classification ⁷ :</p> <p>C07D 401/04, A61K 31/415, 31/47, 31/445, 31/44, 31/50, 31/505, 31/52, C07D 405/14, 401/14, 409/14, 403/04, 487/04, 473/00, 413/14, 417/14, 471/04, A61P 29/00 // (C07D 487/04, 293:00, 231:00) (C07D 471/04, 221:00, 209:00)</p>	A1	<p>(11) International Publication Number: WO 00/31063</p> <p>(43) International Publication Date: 2 June 2000 (02.06.00)</p>
<p>(21) International Application Number: PCT/US99/26007</p> <p>(22) International Filing Date: 17 November 1999 (17.11.99)</p> <p>(30) Priority Data: 09/196,623 20 November 1998 (20.11.98) US</p> <p>(71) Applicant (for all designated States except US): G.D. SEARLE & CO. [US/US]; Corporate Patent Dept., P.O. Box 5110, Chicago, IL 60680-5110 (US).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): ANANTANARAYAN, Ashok [US/US]; 54 Lisk Drive, Hainesville, IL 60030 (US). CLARE, Michael [GB/US]; 5154 West Brown Street, Skokie, IL 60077 (US). COLLINS, Paul, W. [US/US]; 2317 Carillon Drive, Grayslake, IL 60030 (US). CRICH, Joyce, Z. [US/US]; 1501 G. Topp Lane, Glenview, IL 60025 (US). DEVRAJ, Rajesh [IN/US]; 1331 Oak Borough Drive, Ballwin, MO 63021 (US). FLYNN, Daniel, L. [US/US]; One Amgen Center Drive, Thousand Oaks, CA 91320 (US). GENG, Lifeng [CN/US]; 5300 Davis Street, Skokie, IL 60077 (US). GRANETO, Matthew, J. [US/US]; 352 Hartwell Court, Chesterfield, MO 63017 (US). HANAU, Cathleen, E. [US/US]; 15551 Wendimill Drive, Chesterfield, MO 63017 (US). HANSON, Gunnar, J. [US/US]; 7410 Keystone Avenue, Skokie, IL 60077 (US). HARTMANN, Susan, J. [US/US]; 613 West Essex Avenue, Kirkwood, MO 63122 (US). HEPERLE, Michael [DE/US]; 1460 Keystone Court, St. Charles, MO 63303 (US). HUANG, He [CN/US]; 2309F S. Stewart Avenue, Chicago, IL 60616 (US). KHANNA, Ish, K. [CN/US]; 1821 S. Falcon Drive, Libertyville, IL 60048 (US). KOSZYK, Francis, J. [US/US]; 11 Wildwood Drive South, Prospect Heights,</p>	<p>IL 60070 (US). LIAO, Shuyuan [US/US]; 1536 Walters Avenue, Northbrook, IL 60062 (US). METZ, Suzanne [US/US]; 525 Westernmill Drive, Chesterfield, MO 63017 (US). PARTIS, Richard, A. [US/US]; 2221 Noyes Street, Evanston, IL 60201 (US). PERRY, Thao, D. [US/US]; 516 Bloom Street, Red Bud, IL 62278 (US). RAO, Shashidhar, N. [IN/US]; 736 Bellerive Manor Drive, St. Louis, MO 63141 (US). SELNESS, Shaun, Raj [US/US]; 1875 Cedarmill Drive, Chesterfield, MO 63017 (US). SOUTH, Michael, S. [US/US]; 11671 Cheiftain Drive, Chesterfield, MO 63146 (US). STEALEY, Michael, A. [US/US]; 502 Juniper Parkway, Libertyville, IL 60048 (US). TALLEY, John, Jeffrey [US/US]; 4701 Clifton Avenue, St. Louis, MO 63109 (US). VAZQUEZ, Michael, L. [US/US]; 614 Castle Meadows Court, Ballwin, MO 63021 (US). WEIER, Richard, M. [US/US]; 240 Hickory Court, Lake Bluff, IL 60044 (US). XU, Xiangdong [CN/US]; 7498 Abbey Road, Gurnee, IL 60031 (US). YU, Yi [CN/US]; 9065 Grosse Point Road, Skokie, IL 60077 (US).</p> <p>(74) Agents: SCRIVNER, Alan, L. et al.; G.D. Searle & Co., Corporate Patent Dept., P.O. Box 5110, Chicago, IL 60680-5110 (US).</p> <p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</p>	
<p>(54) Title: SUBSTITUTED PYRAZOLES AS p38 KINASE INHIBITORS</p> <div style="text-align: center;">  <p>(IA)</p> </div> <p>(57) Abstract</p> <p>A class of pyrazole derivatives is described for use in treating p38 kinase mediated disorders. Compounds of particular interest are defined by Formula (IA), wherein R¹, R², R³ and R⁴ are as described in the specification.</p>		

129

1089

WHAT IS CLAIMED IS:

1. A compound of Formula IB:



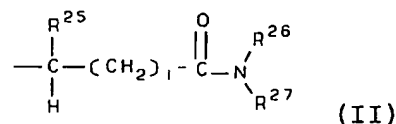
wherein

- 5 R^1 is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxy carbonyl, alkoxy carbonylalkylene, aryloxy carbonylalkylene, heterocycliloxy carbonylalkylene, alkoxy carbonylarylene, aryloxy carbonylarylene, heterocycliloxy carbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,

1090

- 30 arylcarbonyloxyarylene, and
heterocyclylcarbonyloxyarylene; or

R¹ has the formula



wherein:

- 35 i is an integer from 0 to 9;

R²⁵ is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and

- 40 heterocyclylcarbonylaminoalkylene; and

R²⁶ is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxyalkylene, and alkylaminoalkyl; and

- R²⁷ is selected from alkyl, cycloalkyl, alkynyl,
45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene,
50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxyalkoxyalkylene, alkoxyalkoxyheterocyclyl,
55 alkoxyalkoxyheterocyclylcarbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxyalkoxyarylene,
60 aryloxyalkoxyarylene, alkylaryloxyalkoxyarylene, arylcarbonylarylene, alkylarylcabonylarylene, alkoxyalkoxyheterocyclylarylene,

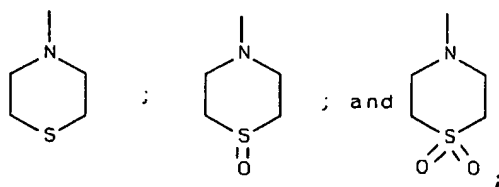
1091

alkoxycarbonylalkoxylarylene,
heterocyclylcarbonylalkylarylene, alkylthioalkylene,
65 cycloalkylthioalkylene, alkylthioarylene,
aralkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, arylsulfonylaminoalkylene,
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
70 heterocyclylalkylene, alkylheterocyclylarylene,
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
aryloxycarbonylarylene, arylcarbonylarylene,
alkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, and alkylsulfonylarylene groups
75 may be optionally substituted with one or more radicals
independently selected from alkyl, halo, haloalkyl,
alkoxy, keto, amino, nitro, and cyano; or
R²⁷ is -CHR²⁸R²⁹ wherein R²⁸ is alkoxycarbonyl, and R²⁹
is selected from aralkyl, aralkoxyalkylene,
80 heterocyclylalkylene, alkylheterocyclylalkylene,
alkoxycarbonylalkylene, alkylthioalkylene, and
aralkylthioalkylene; wherein said aralkyl and
heterocyclyl groups may be optionally substituted with
one or more radicals independently selected from alkyl
85 and nitro; or
R²⁶ and R²⁷ together with the nitrogen atom to which
they are attached form a heterocycle, wherein said
heterocycle is optionally substituted with one or more
radicals independently selected from alkyl, aryl,
90 heterocyclyl, heterocyclylalkylene,
alkylheterocyclylalkylene, aryloxyalkylene,
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
alkoxycarbonylamino; wherein said aryl,
95 heterocyclylalkylene and aryloxyalkylene radicals may be
optionally substituted with one or more radicals
independently selected from halogen, alkyl and alkoxy;
and

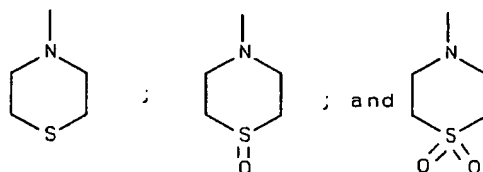
1092

R^2 is piperidinyl substituted with one or more
100 substituents selected from hydroxyalkyl, hydroxyalkenyl,
hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene,
alkoxyalkynylene, and hydroxyacyl, wherein said
hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl,
alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, and
105 hydroxyacyl substituents may be optionally substituted
with one or more substituents selected from cycloalkyl,
alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl,
wherein said cycloalkyl, alkyl, aryl, arylalkyl,
haloalkyl, and heteroarylalkyl substituents may be
110 optionally substituted with one or more substituents
selected from alkylene, alkynylene, hydroxy, halo,
haloalkyl, alkoxy, keto, amino, nitro, cyano,
alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,
aryloxy, heterocyclyl, and heteroaralkoxy; or
115 R^2 is piperidinyl substituted with one or more
substituents selected from hydroxycycloalkyl and
alkoxycycloalkyl, and wherein said hydroxycycloalkyl and
alkoxycycloalkyl substituents may be optionally
substituted with one or more substituents selected from
120 cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and
heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl,
arylalkyl, haloalkyl, and heteroarylalkyl substituents
may be optionally substituted with one or more
substituents selected from alkylene, alkynylene, hydroxy,
125 halo, haloalkyl, alkoxy, keto, amino, nitro, cyano,
alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,
aryloxy, heterocyclyl, and heteroaralkoxy; and
 R^3 is selected from pyridinyl, pyrimidinyl,
quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,
130 thiazolylalkyl, thiazolylamino,

1093



wherein the R³ pyridinyl, pyrimidinyl, quinolinyl,
 purinyl, maleimidyl, pyridonyl, thiazolyl,
 135 thiazolylalkyl, thiazolylamino,



groups may be optionally substituted with one or more
 substituents independently selected from hydrogen, aryl,
 140 alkylamino, alkylthio, alkylloxy, aryloxy, arylamino,
 arylthio, aralkoxy, wherein said aryl, alkylamino,
 alkylthio, alkylloxy, aryloxy, arylamino, arylthio,
 aralkoxy substituents may be optionally substituted with
 one or more alkylene, alkenylene, hydroxy, halo,
 145 haloalkyl, alkoxy, keto, amino, nitro, cyano,
 alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,
 aryloxy, heterocyclyl, and heteroaralkoxy; and

R⁴ is selected from hydrido, alkyl, alkenyl, alkynyl,
 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
 150 R⁴ is optionally substituted with one or more substituents
 independently selected from halo, haloalkyl, haloalkoxy,
 alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl,
 wherein said haloalkyl, haloalkoxy, alkoxy, cyano,
 hydroxy, alkyl, alkenyl, and alkynyl substituents may be
 155 optionally substituted with one or more alkylene,
 alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy,
 keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl,
 alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and
 heteroaralkoxy; or

160 a pharmaceutically-acceptable salt or tautomer

thereof.

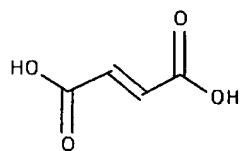
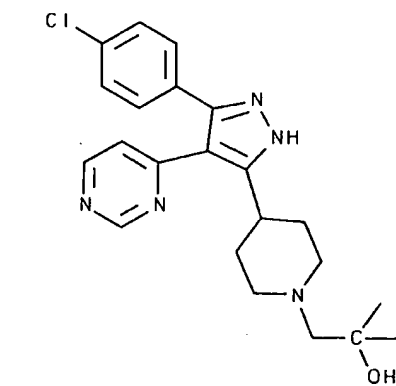
2. A compound of Claim 1 wherein:

R^2 is piperidinyl substituted with one or more substituents selected from hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, hydroxyalkylcarbonyl, hydroxyalkenylcarbonyl, and hydroxyalkynylcarbonyl, wherein said hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, hydroxyalkylcarbonyl, hydroxyalkenylcarbonyl, and hydroxyalkynylcarbonyl substituents may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

R^2 is piperidinyl substituted with one or more substituents selected from hydroxycycloalkyl, alkoxycycloalkyl, and hydroxycycloalkylcarbonyl, wherein said hydroxycycloalkyl, alkoxycycloalkyl, and hydroxycycloalkylcarbonyl substituents may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy.

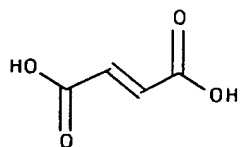
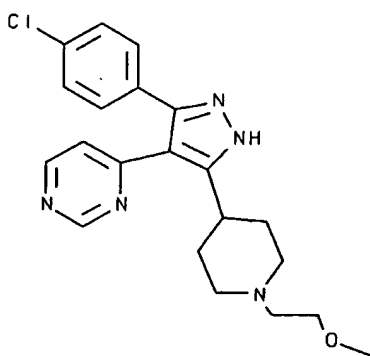
1095

3. A compound of Claim 1 selected from compounds, their tautomers and their pharmaceutically acceptable salts, of the group consisting of:



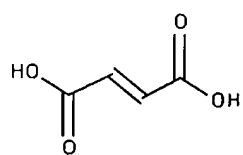
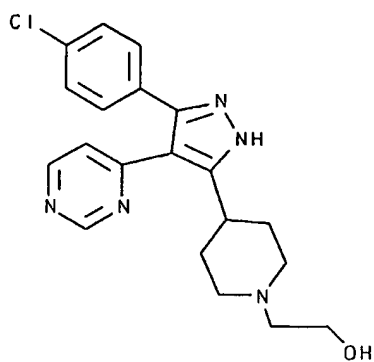
;

5

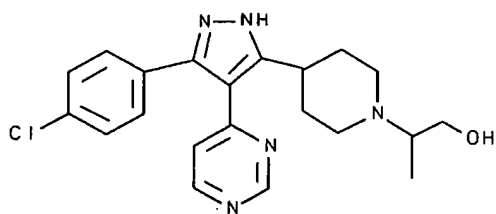


;

1096

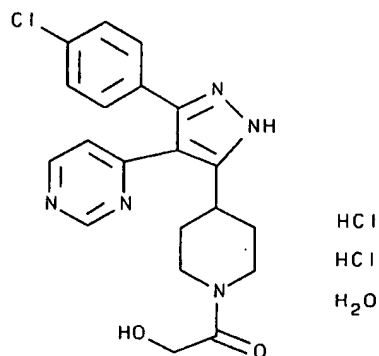


;

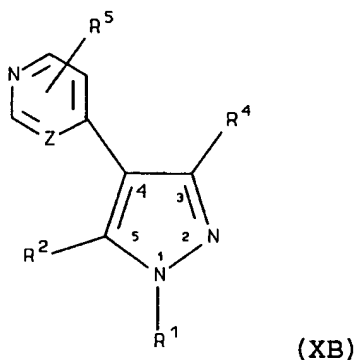


; and

1097



4. A compound of Claim 1 having Formula XB:



wherein

Z represents a carbon atom or a nitrogen atom;

R¹ is selected from hydrido, hydroxy, alkyl,
 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl,
 heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene,
 heterocyclylalkylene, haloalkyl, haloalkenyl,
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,

alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl,
 heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl,
 alkylthioalkylene, alkenylthioalkylene,
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,
 15 alkenylamino, alkynylamino, arylamino, heterocyclylamino,
 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,
 arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
 heterocyclylsulfonyl, alkylaminoalkylene,
 20 alkylsulfonylalkylene, acyl, acyloxycarbonyl,
 alkoxycarbonylalkylene, aryloxycarbonylalkylene,
 heterocyclyloxycarbonylalkylene, alkoxycarbonylarylene,
 aryloxycarbonylarylene, heterocyclyloxycarbonylarylene,
 alkylcarbonylalkylene, arylcarbonylalkylene,
 25 heterocyclylcarbonylalkylene, alkylcarbonylarylene,
 arylcarbonylarylene, heterocyclylcarbonylarylene,
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 arylcarbonyloxyarylene, and
 30 heterocyclylcarbonyloxyarylene; and

R^2 is piperidinyl substituted with one or more
 substituents selected from hydroxyalkyl, hydroxyalkenyl,
 alkoxyalkylene, alkoxyalkenylene, hydroxyalkylcarbonyl,
 and hydroxyalkenylcarbonyl, wherein said hydroxyalkyl,
 35 hydroxyalkenyl, alkoxyalkylene, alkoxyalkenylene,
 hydroxyalkylcarbonyl, and hydroxyalkenylcarbonyl
 substituents may be optionally substituted with one or
 more substituents selected from cycloalkyl, alkyl, aryl,
 arylalkyl, haloalkyl, and heteroarylalkyl, wherein said
 40 cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and
 heteroarylalkyl substituents may be optionally
 substituted with one or more substituents selected from
 alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy,
 keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl,
 45 alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and
 heteroaralkoxy; or

R² is piperidinyl substituted with one or more substituents selected from hydroxycycloalkyl and hydroxycycloalkylcarbonyl, wherein said hydroxycycloalkyl and hydroxycycloalkylcarbonyl substituents may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

R⁴ is selected from cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R⁴ is optionally substituted with one or more substituents independently selected from halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

R⁵ represents one or more substituents independently selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

a pharmaceutically-acceptable salt or tautomer

1100

thereof.

5. A compound of Claim 4 wherein R² is piperidinyl substituted with at least one substituent attached to the distal nitrogen heteroatom or to a carbon ring atom adjacent to the distal nitrogen heteroatom of the piperidine ring.

6. A compound of Claim 4 wherein Z represents a carbon atom.

7. A compound of Claim 4 wherein Z represents a nitrogen atom.

8. A compound of Claim 4 wherein R¹ is selected from hydrido, alkyl, hydroxyalkyl and alkynyl.

9. A compound of Claim 4 wherein R¹ is hydrido.

10. A compound of Claim 4 wherein R² is piperidinyl substituted with at least one substituent selected from lower hydroxyalkyl, lower hydroxyalkylcarbonyl and hydroxycycloalkylcarbonyl.

11. A compound of Claim 4 wherein R⁴ is optionally substituted phenyl.

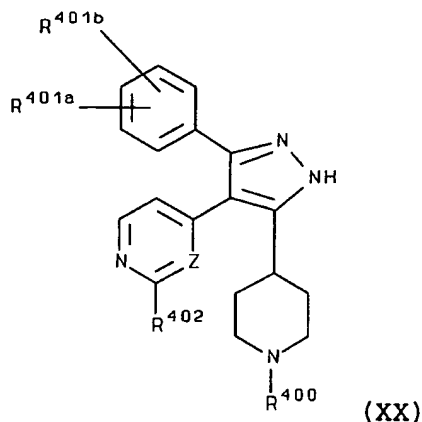
12. A compound of Claim 4 wherein R⁴ is phenyl optionally substituted at a substitutable position with one or more radicals independently selected from chloro, fluoro, bromo and iodo.

13. A compound of Claim 4 wherein R⁴ is phenyl optionally substituted at the meta or para position with one or more chloro radicals.

1101

14. A compound of Claim 4 wherein R⁵ is hydrido.

15. A compound of Claim 1 having Formula XX:



wherein:

Z represents a carbon atom or a nitrogen atom;

5 R⁴⁰⁰ is selected from hydroxyalkyl,
hydroxyalkylcarbonyl and alkoxyalkylene, wherein said
hydroxyalkyl, hydroxyalkylcarbonyl and alkoxyalkylene may
be optionally substituted with one or more substituents
selected from cycloalkyl, alkyl, aryl, arylalkyl,
10 haloalkyl, and heteroarylalkyl, wherein said cycloalkyl,
alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl
substituents may be optionally substituted with one or
more substituents selected from alkylene, alkynylene,
hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro,
15 cyano, alkylsulfonyl, alkylsulfinyl, alkylthio,
alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy;
or

 R⁴⁰⁰ is hydroxycycloalkylcarbonyl that is optionally
substituted with one or more substituents selected from
20 cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and

1102

heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

R^{401a} and R^{401b} are independently selected from hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

R⁴⁰² is selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

a pharmaceutically-acceptable salt or tautomer thereof.

16. A compound of Claim 15 wherein:

R⁴⁰⁰ is selected from lower hydroxyalkyl, lower hydroxyalkylcarbonyl and lower alkoxyalkylene, wherein said lower hydroxyalkyl, lower hydroxyalkylcarbonyl and lower alkoxyalkylene may be optionally substituted with one or more substituents selected from cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and

1103

lower heteroarylalkyl, wherein said cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from lower alkylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or

R⁴⁰⁰ is hydroxycycloalkylcarbonyl that is optionally substituted with one or more substituents selected from cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl, wherein said cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from lower alkylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, aryloxy, heterocyclyl, and lower heteroaralkoxy; and

R^{401a} and R^{401b} are independently selected from hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and

R⁴⁰² is selected from hydrogen, phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said

1104

phenyl, lower alkylamino, lower alkylthio, lower
alkyloxy, phenyloxy, phenylamino, phenylthio, and
45 phenylalkoxy may be optionally substituted with one or
more lower alkylene, lower alkenylene, hydroxy, halo,
lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano,
lower alkylsulfonyl, lower alkylsulfinyl, lower
alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl,
50 and lower heteroaralkoxy; or
a pharmaceutically-acceptable salt or tautomer
thereof.

17. A compound of Claim 15 wherein Z represents a
carbon atom.

18. A compound of Claim 15 wherein Z represents a
nitrogen atom.

19. A compound of Claim 15 wherein R⁴⁰⁰ is
optionally substituted hydroxyalkylcarbonyl.

20. A compound of Claim 15 wherein R⁴⁰⁰ is
optionally substituted hydroxycycloalkylcarbonyl.

21. A compound of Claim 15 wherein R⁴⁰⁰ is
optionally substituted alkoxyalkylene.

22. A compound of Claim 15 wherein R⁴⁰⁰ is
optionally substituted hydroxyalkyl.

23. A compound of Claim 15 wherein R⁴⁰¹ represents
one or more chloro, fluoro, bromo and iodo.

24. A compound of Claim 15 wherein R⁴⁰¹ is meta-
chloro or para-chloro.

25. A compound of Claim 15 wherein R⁴⁰² is hydrido.

1105

26. A compound of Claim 15 wherein:

R⁴⁰⁰ is optionally substituted lower
hydroxyalkylcarbonyl;

5 R^{401a} is selected from chloro, fluoro, bromo and iodo;
and
R⁴⁰² is hydrido.

27. A compound of Claim 15 wherein:

R⁴⁰⁰ is selected from optionally substituted 2-
hydroxyacetyl, 2-hydroxy-propionyl, 2-hydroxy-2-
methylpropionyl, 2-hydroxy-2-phenylacetyl, 3-
5 hydroxypropionyl, 2-hydroxy-3-methylbutyryl, 2-
hydroxyisocaproyl, 2-hydroxy-3-phenylpropionyl, and 2-
hydroxy-3-imidazolylpropionyl;

10 R^{401a} is selected from chloro, fluoro, bromo and iodo;
and
R⁴⁰² is hydrido.

28. A compound of Claim 27 wherein R^{401a} is meta-
chloro or para-chloro.

29. A compound of Claim 27 wherein R^{401a} is para-
chloro and R^{401b} is hydrogen.

30. A compound of Claim 15 wherein:

R⁴⁰⁰ is optionally substituted lower
hydroxycycloalkylcarbonyl;

5 R^{401a} is selected from chloro, fluoro, bromo and iodo;
and
R⁴⁰² is hydrido.

31. A compound of Claim 15 wherein:

R⁴⁰⁰ is selected from optionally substituted 1-
hydroxy-1-cyclohexylacetyl, 2-hydroxy-1-cyclohexylacetyl,
3-hydroxy-1-cyclohexylacetyl, 4-hydroxy-1-
5 cyclohexylacetyl, 1-hydroxy-1-cyclopentylacetyl, 2-

1106

hydroxy-1-cyclopentylacetyl, and 3-hydroxy-1-cyclopentylacetyl, 2-hydroxy-2-cyclohexylacetyl;

R^{401a} is selected from chloro, fluoro, bromo and iodo;
and

10 R⁴⁰² is hydrido.

32. A compound of Claim 31 wherein R^{401a} is meta-chloro or para-chloro.

33. A compound of Claim 15 wherein:

R⁴⁰⁰ is optionally substituted lower hydroxyalkyl;

R⁴⁰¹ is selected from chloro, fluoro, bromo and iodo;

and

5 R⁴⁰² is hydrido.

34. A compound of Claim 15 wherein:

R⁴⁰⁰ is selected from optionally substituted hydroxymethyl, hydroxyethyl, hydroxypropyl and hydroxyisopropyl;

5 R^{401a} is selected from chloro, fluoro, bromo and iodo;
and

R⁴⁰² is hydrido.

35. A compound of Claim 34 wherein R^{401a} is meta-chloro or para-chloro.

36. A compound of Claim 15 wherein:

R⁴⁰⁰ is optionally substituted lower alkoxyalkylene;

R^{401a} is selected from chloro, fluoro, bromo and iodo;

and

5 R⁴⁰² is hydrido.

37. A compound of Claim 15 wherein:

R⁴⁰⁰ is selected from optionally substituted methoxymethylene, methoxyethylene, methoxypropylene, methoxyisopropylene, ethoxymethylene, ethoxyethylene,

1107

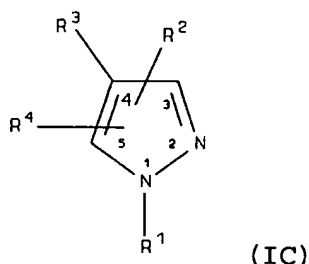
5 ethoxypropylene, and ethoxyisopropylene.

R^{401a} is selected from chloro, fluoro, bromo and iodo;
and

R^{402} is hydrido.

38. A compound of Claim 37 wherein R^{401a} is meta-chloro or para-chloro.

39. A compound of Formula IC:



5 wherein

R^1 is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxy carbonylalkylene, aryloxycarbonylalkylene,

10

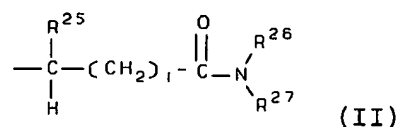
15

20

1108

heterocyclyloxy carbonylalkylene, alkoxycarbonylarylene,
 25 aryloxy carbonylarylene, heterocyclyloxy carbonylarylene,
 alkylcarbonylalkylene, arylcarbonylalkylene,
 heterocyclylcarbonylalkylene, alkylcarbonylarylene,
 arylcarbonylarylene, heterocyclylcarbonylarylene,
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 30 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 arylcarbonyloxyarylene, and
 heterocyclylcarbonyloxyarylene; or

R¹ has the formula



35 wherein:

i is an integer from 0 to 9;

R²⁵ is selected from hydrogen, alkyl, aralkyl,
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
 40 alkylcarbonylalkylene, arylcarbonylalkylene, and
 heterocyclylcarbonylaminoalkylene; and

R²⁶ is selected from hydrogen, alkyl, alkenyl,
 alkynyl, cycloalkylalkylene, aralkyl,
 alkoxycarbonylalkylene, and alkylaminoalkyl; and

45 R²⁷ is selected from alkyl, cycloalkyl, alkynyl,
 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,
 cycloalkenylalkylene, cycloalkylarylene,
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,
 50 alkylheterocyclylalkylene, alkylheterocyclylarylene,
 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,
 alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,
 aryloxyarylene, aralkoxyarylene,
 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,
 55 alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl,
 alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl,

alkylaminoalkylene, arylaminocarbonylalkylene,
alkoxyarylaminoalkylene, aminocarbonylalkylene,
arylaminocarbonylalkylene, alkylaminocarbonylalkylene,
60 arylcarbonylalkylene, alkoxycarbonylarylene,
aryloxyalkylene, alkylaryloxyalkylene,
arylcarbonylarylene, alkylarylcarbonylarylene,
alkoxycarbonylheterocyclylarylene,
alkoxycarbonylalkoxyalkylene,
65 heterocyclylcarbonylalkylarylene, alkylthioalkylene,
cycloalkylthioalkylene, alkylthioarylene,
aralkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, arylsulfonylaminoalkylene,
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
70 said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
heterocyclylalkylene, alkylheterocyclylarylene,
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
aryloxyalkylene, arylcarbonylarylene,
alkylthioarylene, heterocyclylthioarylene,
75 arylthioalkylarylene, and alkylsulfonylarylene groups
may be optionally substituted with one or more radicals
independently selected from alkyl, halo, haloalkyl,
alkoxy, keto, amino, nitro, and cyano; or

R^{27} is $-CHR^{28}R^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
80 is selected from aralkyl, aralkoxyalkylene,
heterocyclylalkylene, alkylheterocyclylalkylene,
alkoxycarbonylalkylene, alkylthioalkylene, and
aralkylthioalkylene; wherein said aralkyl and
heterocyclyl groups may be optionally substituted with
85 one or more radicals independently selected from alkyl
and nitro; or

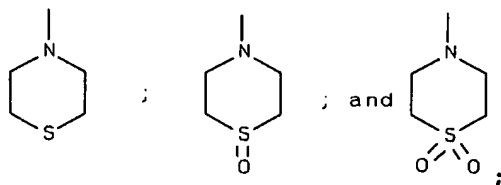
R^{26} and R^{27} together with the nitrogen atom to which
they are attached form a heterocycle, wherein said
heterocycle is optionally substituted with one or more
90 radicals independently selected from alkyl, aryl,
heterocyclyl, heterocyclylalkylene,
alkylheterocyclylalkylene, aryloxyalkylene,

1110

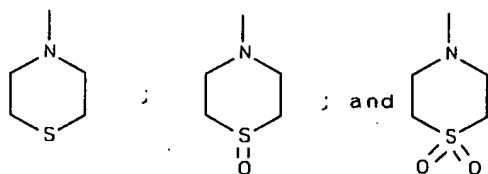
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
 alkoxy carbonyl, aralkoxy carbonyl, alkylamino and
 95 alkoxy carbonylamino; wherein said aryl,
 heterocyclalkylene and aryloxyalkylene radicals may be
 optionally substituted with one or more radicals
 independently selected from halogen, alkyl and alkoxy;
 and

100 R² is cyclohexyl substituted with one or more
 substituents selected from optionally substituted
 hydroxyalkyl, alkylaminoalkylene and cycloalkylamino; and

R³ is selected from pyridinyl, pyrimidinyl,
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,
 105 thiazolylalkyl, thiazolylamino,



wherein the R³ pyridinyl, pyrimidinyl, quinolinyl,
 purinyl, maleimidyl, pyridonyl, thiazolyl,
 110 thiazolylalkyl, thiazolylamino,

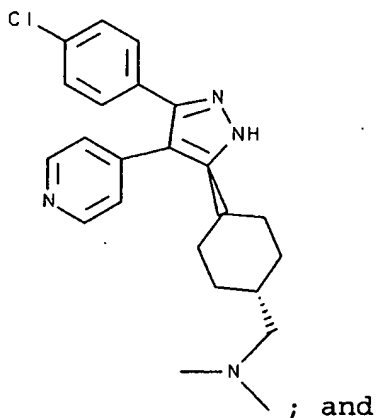


groups may be optionally substituted with one or more
 substituents independently selected from hydrogen, aryl,
 115 alkylamino, alkylthio, alkyloxy, aryloxy, arylamino,
 arylthio, aralkoxy, wherein said aryl, alkylamino,
 alkylthio, alkyloxy, aryloxy, arylamino, arylthio,
 aralkoxy substituents may be optionally substituted with
 one or more alkylene, alkenylene, hydroxy, halo,
 120 haloalkyl, alkoxy, keto, amino, nitro, cyano,
 alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,
 aryloxy, heterocyclyl, and heteroaralkoxy; and

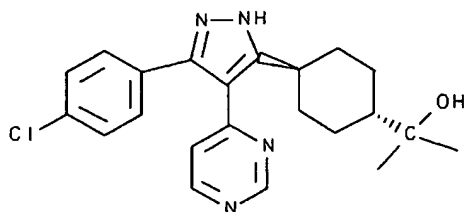
1111

R⁴ is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
125 R⁴ is optionally substituted with one or more substituents independently selected from halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl substituents may be
130 optionally substituted with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or
135 a pharmaceutically-acceptable salt or tautomer thereof.

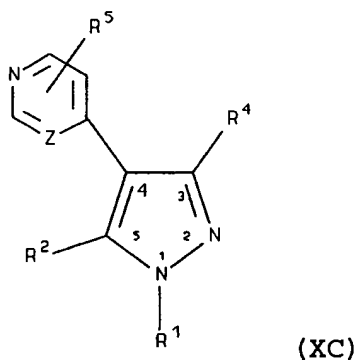
40. A compound of Claim 39 selected from compounds, their tautomers and their pharmaceutically acceptable salts, of the group consisting of :



1112



41. A compound of Claim 39 having Formula XC:



wherein

Z represents a carbon atom or a nitrogen atom;

- R¹ is selected from hydrido, hydroxy, alkyl,
 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl,
 heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene,
 heterocyclylalkylene, haloalkyl, haloalkenyl,
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,
 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl,
 heterocyclloxyalkyl, alkoxyalkoxy, mercaptoalkyl,
 alkylthioalkylene, alkenylthioalkylene,
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,
 15 alkenylamino, alkynylamino, arylamino, heterocyclylamino,

1113

- alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,
arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,
alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
heterocyclylsulfonyl, alkylaminoalkylene,
20 alkylsulfonylalkylene, acyl, acyloxycarbonyl,
alkoxycarbonylalkylene, aryloxycarbonylalkylene,
heterocyclylloxycarbonylalkylene, alkoxycarbonylarylene,
aryloxycarbonylarylene, heterocyclylloxycarbonylarylene,
alkylcarbonylalkylene, arylcarbonylalkylene,
25 heterocyclylcarbonylalkylene, alkylcarbonylarylene,
arylcarbonylarylene, heterocyclylcarbonylarylene,
alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
arylcarbonyloxyarylene, and
30 heterocyclylcarbonyloxyarylene; and
R² is cyclohexyl substituted with one or more
substituents selected from optionally substituted
hydroxyalkyl, alkylaminoalkylene and cycloalkylamino; and
R⁴ is selected from cycloalkyl, cycloalkenyl, aryl,
35 and heterocyclyl, wherein R⁴ is optionally substituted
with one or more substituents independently selected from
halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy,
alkyl, alkenyl, and alkynyl, wherein said haloalkyl,
haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl
40 substituents may be optionally substituted with one or
more alkylene, alkenylene, alkynylene, hydroxy, halo,
haloalkyl, alkoxy, keto, amino, nitro, cyano,
alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,
aryloxy, heterocyclyl, and heteroaralkoxy; and
45 R⁵ represents one or more substituents independently
selected from hydrogen, aryl, alkylamino, alkylthio,
alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein
said aryl, alkylamino, alkylthio, alkyloxy, aryloxy,
arylamino, arylthio, aralkoxy substituents may be
50 optionally substituted with one or more alkylene,
alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto,

1114

amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

55 a pharmaceutically-acceptable salt or tautomer thereof.

42. A compound of Claim 41 wherein R² is cyclohexyl substituted with at least one substituent attached to the 4-position carbon ring atom of the cyclohexyl ring.

43. A compound of Claim 41 wherein Z represents a carbon atom.

44. A compound of Claim 41 wherein Z represents a nitrogen atom.

45. A compound of Claim 41 wherein R¹ is selected from hydrido, alkyl, hydroxyalkyl and alkynyl.

46. A compound of Claim 41 wherein R¹ is hydrido.

47. A compound of Claim 41 wherein R² is cyclohexyl substituted with one or more substituents selected from optionally substituted lower hydroxyalkyl, lower alkylaminoalkylene and cycloalkylamino.

48. A compound of Claim 41 wherein R⁴ is optionally substituted phenyl.

49. A compound of Claim 41 wherein R⁴ is phenyl optionally substituted at a substitutable position with one or more radicals independently selected from chloro, fluoro, bromo and iodo.

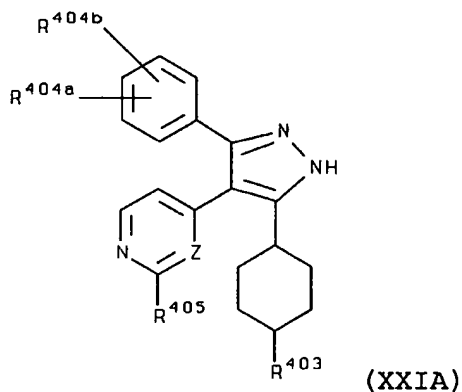
50. A compound of Claim 41 wherein R⁴ is phenyl optionally substituted at the meta or para position with

1115

one or more chloro radicals.

51. A compound of Claim 41 wherein R⁵ is hydrido.

52. A compound of Claim 41 having Formula XXIA:



wherein:

Z represents a carbon atom or a nitrogen atom;

R⁴⁰³ is selected from hydroxyalkyl,

5 alkylaminoalkylene and cycloalkylamino; and

R^{404a} and R^{404b} are independently selected from
hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano,
hydroxy, alkyl, alkenyl, and alkynyl, wherein said
haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl,
10 and alkynyl substituents may be optionally substituted
with one or more alkylene, alkenylene, alkynylene,
hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro,
cyano, alkylsulfonyl, alkylsulfinyl, alkylthio,
alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy;
15 and

R⁴⁰⁵ is selected from hydrogen, aryl, alkylamino,
alkylthio, alkyloxy, aryloxy, arylamino, arylthio,
aralkoxy, wherein said aryl, alkylamino, alkylthio,
alkyloxy, aryloxy, arylamino, arylthio, aralkoxy

1116

- 20 substituents may be optionally substituted with one or more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or
- 25 a pharmaceutically-acceptable salt or tautomer thereof.

53. A compound of Claim 52 wherein:

- R^{403} is selected from lower hydroxyalkyl, lower alkylaminoalkylene and cycloalkylamino; and
- R^{404a} and R^{404b} are independently selected from hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and
- 15 R^{405} is selected from hydrogen, phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or more lower alkylene, lower alkenylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or
- 20 a pharmaceutically-acceptable salt or tautomer thereof.

1117

54. A compound of Claim 52 wherein Z represents a carbon atom.

55. A compound of Claim 52 wherein Z represents a nitrogen atom.

56. A compound of Claim 52 wherein R⁴⁰³ is optionally substituted hydroxyalkyl.

57. A compound of Claim 52 wherein R⁴⁰³ is optionally substituted alkylaminoalkylene.

58. A compound of Claim 57 wherein R⁴⁰³ is optionally substituted dialkylaminoalkylene.

59. A compound of Claim 52 wherein R⁴⁰³ is optionally substituted cycloalkylamino.

60. A compound of Claim 52 wherein R^{404a} is selected from chloro, fluoro, bromo and iodo.

61. A compound of Claim 52 wherein R^{404a} is meta-chloro or para-chloro.

62. A compound of Claim 52 wherein R⁴⁰⁵ is hydrido.

63. A compound of Claim 52 wherein:
R⁴⁰³ is optionally substituted lower hydroxyalkyl;
R^{404a} is selected from chloro, fluoro, bromo and iodo;

5 and

R⁴⁰⁵ is hydrido.

64. A compound of Claim 52 wherein:

R⁴⁰³ is selected from optionally substituted hydroxymethyl, hydroxyethyl, hydroxypropyl and hydroxybutyl;

1118

5 R^{404a} is selected from chloro, fluoro, bromo and iodo;
and

R^{405} is hydrido.

65. A compound of Claim 64 wherein R^{404a} is meta-chloro or para-chloro.

66. A compound of Claim 52 wherein:

R^{403} is optionally substituted lower
alkylaminoalkylene;

5 R^{404a} is selected from chloro, fluoro, bromo and iodo;
and

R^{405} is hydrido.

67. A compound of Claim 52 wherein:

R^{403} is selected from optionally substituted
methylaminomethylene, methylaminoethylene,
methylaminopropylene, ethylaminomethylene,
5 ethylaminoethylene, ethylaminopropylene,
propylaminomethylene, propylaminoethylene,
propylaminopropylene, dimethylaminomethylene,
dimethylaminoethylene, dimethylaminopropylene,
diethylaminomethylene, diethylaminoethylene,
10 diethylaminopropylene, dipropylaminomethylene,
dipropylaminoethylene, and dipropylaminopropylene;

R^{404a} is selected from chloro, fluoro, bromo and iodo;
and

R^{405} is hydrido.

68. A compound of Claim 67 wherein R^{404a} is meta-chloro or para-chloro.

69. A compound of Claim 52 wherein:

R^{403} is optionally substituted cycloalkylamino;

R^{404a} is selected from chloro, fluoro, bromo and iodo;
and

1119

5 R^{405} is hydrido.

70. A compound of Claim 52 wherein:

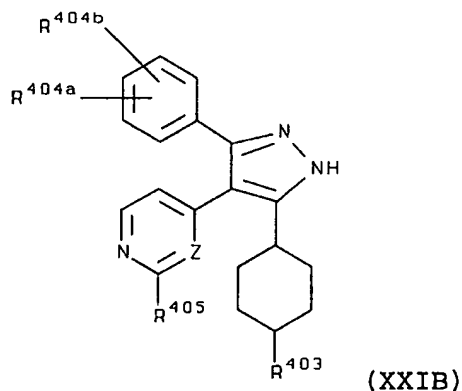
R^{403} is selected from optionally substituted
cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl;

R^{404a} is selected from chloro, fluoro, bromo and iodo;

5 and

R^{405} is hydrido.

71. A compound of Formula XXIB:



wherein:

Z represents a carbon atom or a nitrogen atom;

R^{403} is selected from alkylamino; and

5 R^{404a} and R^{404b} are independently selected from

hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano,
hydroxy, alkyl, alkenyl, and alkynyl, wherein said
haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl,
and alkynyl substituents may be optionally substituted
10 with one or more alkylene, alkenylene, alkynylene,
hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro,

1120

cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

- 15 R⁴⁰⁵ is selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or
20 more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or
 a pharmaceutically-acceptable salt or tautomer
25 thereof.

72. A compound of Claim 71 wherein:

 R⁴⁰³ is selected from lower alkylamino; and

- R^{404a} and R^{404b} are independently selected from hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and
5 lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower
10 haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and

- R⁴⁰⁵ is selected from hydrogen, phenyl, lower
15 alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or
20 more lower alkylene, lower alkenylene, hydroxy, halo,

1121

lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or

25 a pharmaceutically-acceptable salt or tautomer thereof.

73. A compound of Claim 71 wherein Z represents a carbon atom.

74. A compound of Claim 71 wherein Z represents a nitrogen atom.

75. A compound of Claim 71 wherein R⁴⁰³ is optionally substituted dialkylamino.

76. A compound of Claim 71 wherein R^{404a} is selected from chloro, fluoro, bromo and iodo.

77. A compound of Claim 71 wherein R^{404a} is meta-chloro or para-chloro.

78. A compound of Claim 71 wherein R⁴⁰⁵ is hydrido.

79. A compound of Claim 71 wherein:

R⁴⁰³ is optionally substituted lower alkylamino;

R^{404a} is selected from chloro, fluoro, bromo and iodo;

and

5 R⁴⁰⁵ is hydrido.

80. A compound of Claim 71 wherein:

R⁴⁰³ is selected from optionally substituted methylamino, ethylamino, n-propylamino, isopropylamino, n-butylamino, sec-butylamino, t-butylamino, isobutylamino, dimethylamino, diethylamino, di-n-propylamino, di-isopropylamino, di-n-butylamino, di-sec-

1122

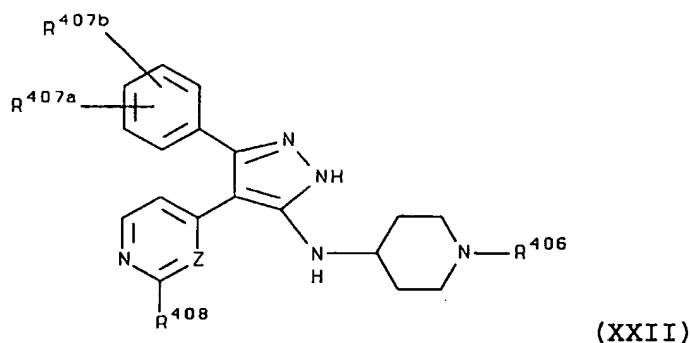
butylamino, di-t-butylamino, and di-isobutylamino;

R^{404a} is selected from chloro, fluoro, bromo and iodo;
and

10 R^{405} is hydrido.

81. A compound of Claim 80 wherein R^{404a} is meta-chloro or para-chloro.

82. A compound Formula XXII:



wherein:

Z represents a carbon atom or a nitrogen atom;

R^{406} is alkynyl; and

5 R^{407a} and R^{407b} are independently selected from hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted
10 with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy;
and

15 R^{408} is selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio,

1123

aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or
20 more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or
a pharmaceutically-acceptable salt or tautomer
25 thereof.

83. A compound of Claim 82 wherein:
R⁴⁰⁶ is selected from lower alkynyl; and
R^{407a} and R^{407b} are independently selected from
hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower
alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and
5 lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower
10 haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and
R⁴⁰⁸ is selected from hydrogen, phenyl, lower
15 alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or
20 more lower alkylene, lower alkenylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or
25 a pharmaceutically-acceptable salt or tautomer

1124

thereof.

84. A compound of Claim 82 wherein Z represents a carbon atom.

85. A compound of Claim 82 wherein Z represents a nitrogen atom.

86. A compound of Claim 82 wherein R^{407a} is selected from chloro, fluoro, bromo and iodo.

87. A compound of Claim 82 wherein R^{407a} is meta-chloro or para-chloro.

88. A compound of Claim 82 wherein R⁴⁰⁸ is hydrido.

89. A compound of Claim 82 wherein:

R⁴⁰⁶ is optionally substituted lower alkynyl;

R^{407a} is selected from chloro, fluoro, bromo and iodo;

and

5 R⁴⁰⁸ is hydrido.

90. A compound of Claim 82 wherein:

R⁴⁰⁶ is selected from optionally substituted ethynyl, propynyl and butynyl;

R^{407a} is selected from chloro, fluoro, bromo and iodo;

5 and

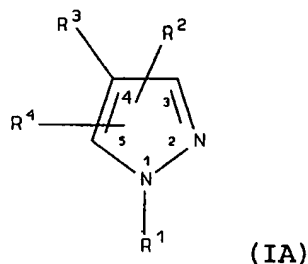
R⁴⁰⁸ is hydrido.

91. A compound of Claim 82 wherein R⁴⁰⁶ is propargyl.

92. A compound of Claim 82 wherein R^{407a} is meta-chloro or para-chloro.

93. A compound of Formula IA

1125

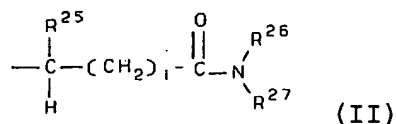


wherein

R¹ is selected from hydrido, hydroxy, alkyl,
 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl,
 heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene,
 heterocyclalkylene, haloalkyl, haloalkenyl,
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,
 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl,
 heterocyclloxyalkyl, alkoxyalkoxy, mercaptoalkyl,
 alkylthioalkylene, alkenylthioalkylene,
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,
 15 alkenylamino, alkynylamino, arylamino, heterocyclylamino,
 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,
 arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
 heterocyclylsulfonyl, alkylaminoalkylene,
 20 alkylsulfonylalkylene, acyl, acyloxycarbonyl,
 alkoxycarbonylalkylene, aryloxycarbonylalkylene,
 heterocyclloxy carbonylalkylene, alkoxycarbonylarylene,
 aryloxycarbonylarylene, heterocyclloxy carbonylarylene,
 alkylcarbonylalkylene, arylcarbonylalkylene,
 25 heterocyclylcarbonylalkylene, alkylcarbonylarylene,
 arylcarbonylarylene, heterocyclylcarbonylarylene,
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 arylcarbonyloxyarylene, and
 30 heterocyclylcarbonyloxyarylene; or

R¹ has the formula

1126



wherein:

i is an integer from 0 to 9;

- 35 R^{25} is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclcarbonylaminoalkylene; and
- 40 R^{26} is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxyalkylene, and alkylaminoalkyl; and
- 45 R^{27} is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocycl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocycl, alkylheterocyclalkylene, alkylheterocyclarylene, aralkylheterocycl, alkoxyalkylene, alkoxyarylene,
- 50 alkoxyaralkyl, alkoxyheterocycl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclalkylene, aryloxyalkoxyarylene, alkoxyalkoxyalkylene, alkoxyalkoxyheterocycl, alkoxyalkoxyheterocyclcarbonylalkylene, aminoalkyl,
- 55 alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxyalkoxyarylene, aryloxyalkoxyarylene, alkylaryloxyalkoxyarylene, arylcarbonylarylene, alkylarylcarbonylarylene,
- 60 alkoxyalkoxyheterocyclarylene, alkoxyalkoxyalkoxyarylene, heterocyclcarbonylalkylarylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene,

1127

- 65 aralkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, arylsulfonylaminoalkylene,
alkylsulfonylarylene, and alkylaminosulfonylarylene;
wherein said alkyl, cycloalkyl, aryl, heterocyclyl,
aralkyl, heterocyclylalkylene, alkylheterocyclylarylene,
70 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
aryloxycarbonylarylene, arylcarbonylarylene,
alkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, and alkylsulfonylarylene groups
may be optionally substituted with one or more radicals
75 independently selected from alkyl, halo, haloalkyl,
alkoxy, keto, amino, nitro, and cyano; or
R²⁷ is -CHR²⁸R²⁹ wherein R²⁸ is alkoxycarbonyl, and R²⁹
is selected from aralkyl, aralkoxyalkylene,
heterocyclylalkylene, alkylheterocyclylalkylene,
80 alkoxycarbonylalkylene, alkylthioalkylene, and
aralkylthioalkylene; wherein said aralkyl and
heterocyclyl groups may be optionally substituted with
one or more radicals independently selected from alkyl
and nitro; or
85 R²⁶ and R²⁷ together with the nitrogen atom to which
they are attached form a heterocycle, wherein said
heterocycle is optionally substituted with one or more
radicals independently selected from alkyl, aryl,
heterocyclyl, heterocyclylalkylene,
90 alkylheterocyclylalkylene, aryloxyalkylene,
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
alkoxycarbonylamino; wherein said aryl,
heterocyclylalkylene and aryloxyalkylene radicals may be
95 optionally substituted with one or more radicals
independently selected from halogen, alkyl and alkoxy;
and
R² is selected from mercapto,
aryl(hydroxyalkyl)amino, N-alkyl-N-alkynyl-amino,
100 aminocarbonylalkylene, alkylcarbonylaminoalkylene,

1128

aminoalkylcarbonylaminoalkylene,
 alkylaminoalkylcarbonylamino, aminoalkylthio,
 alkylaminocarbonylalkylthio,
 alkylaminoalkylaminocarbonylalkylthio, cyanoalkylthio,
 105 alkenylthio, alkynylthio, carboxyalkylthio,
 alkoxyalkylthio, alkylsulfinyl, alkylsulfonyl,
 alkoxyalkyl, alkoxyalkylthio, alkoxyalkylamino,
 alkoxyalkylaminoalkylene, alkoxyalkylaminoalkoxy,
 aralkylthio, heterocyclalkylthio, aminoalkoxy,
 110 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,
 alkenyloxy, alkynyloxy, and heterocyclalkyloxy; or

R^2 is R^{200} -heterocyclalkyl- R^{201} , R^{200} -aryl- R^{201} , or R^{200} -
 cycloalkyl- R^{201} wherein:

R^{200} is selected from:

- 115 - $(CR^{202}R^{203})_y-$;
 - $C(O)-$;
 - $C(O)-(CH_2)_y-$;
 - $C(O)-O-(CH_2)_y-$;
 - $(CH_2)_y-C(O)-$;
 120 - $O-(CH_2)_y-C(O)-$;
 - $NR^{202}-$;
 - $NR^{202}-(CH_2)_y-$;
 - $(CH_2)_y-NR^{202}-$;
 - $(CH_2)_y-NR^{202}-(CH_2)_z-$;
 125 - $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;
 - $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;
 - $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;
 - $S(O)_x-(CR^{202}R^{203})_y-$;
 - $(CR^{202}R^{203})_y-S(O)_x-$;
 130 - $S(O)_x-(CR^{202}R^{203})_y-O-$;
 - $S(O)_x-(CR^{202}R^{203})_y-C(O)-$;
 - $O-(CH_2)_y-$;
 - $(CH_2)_y-O-$;
 - $S-$; and
 135 - $O-$;
 or R^{200} represents a bond;

1129

R^{201} represents one or more radicals selected from the group consisting of hydroxy, hydroxyalkyl, cycloalkyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxyalkylene, alkoxyarylene, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonylalkylene, aminoalkyl, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene, alkylimidocarbonyl, amidino, alkylamidino, aralkylamidino, guanidino, guanidinoalkylene, and alkylsulfonylamino; and

R^{202} and R^{203} are independently selected from hydrido, alkyl, aryl and aralkyl; and

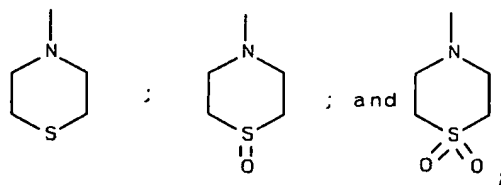
y and z are independently 0, 1, 2, 3, 4, 5 or 6 wherein y + z is less than or equal to 6; and

x is 0, 1 or 2; or

R^2 is $-NHCR^{204}R^{205}$ wherein R^{204} is alkylaminoalkylene, and R^{205} is aryl; or

R^2 is $-C(NR^{206})R^{207}$ wherein R^{206} is selected from hydrogen and hydroxy, and R^{207} is selected from alkyl, aryl and aralkyl; and

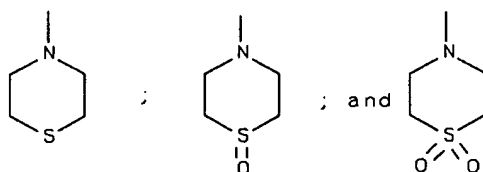
R^3 is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



165

wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,

1130



170

groups may be optionally substituted with one or more radicals independently selected from halo, keto, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloaryl amino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclylloxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$ wherein R^{44} is alkylcarbonyl or amino, and R^{45} is alkyl or aralkyl; and

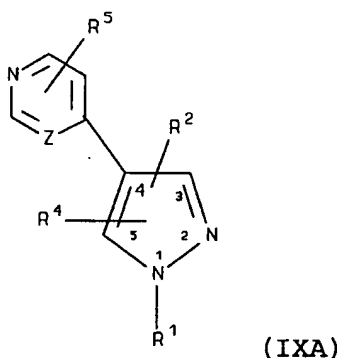
R^4 is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R^4 is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

200

1131

- alkylsulfinylalkylene, arylsulfinylalkylene,
 alkylsulfonyl, alkylsulfonylalkylene,
 205 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
 nitro, alkylamino, arylamino, alkylaminoalkylene,
 arylaminoalkylene, aminoalkylamino, and hydroxy;
 210 provided R^3 is not 2-pyridinyl when R^4 is a phenyl
 ring containing a 2-hydroxy substituent and when R^1 is
 hydrido; and
 further provided R^2 is selected from $-R^{200}-$
 heterocyclyl- R^{201} , $-R^{200}-$ aryl- R^{201} , or $-R^{200}-$ unsubstituted
 215 cycloalkyl- R^{201} when R^4 is hydrido; and
 further provided that R^4 is not methylsulfonylphenyl
 or aminosulfonylphenyl; and
 further provided that R^1 is not methylsulfonylphenyl;
 or
 220 a pharmaceutically-acceptable salt or tautomer
 thereof.

94. A compound of Formula IXA:



wherein

Z represents a carbon atom or a nitrogen atom; and

5 R^1 is selected from hydrido, lower alkyl, lower

1132

hydroxyalkyl, lower alkynyl, lower aralkyl, lower aminoalkyl and lower alkylaminoalkyl; and

R^2 is lower hydroxyalkylamino; or

R^2 is R^{200} -heterocyclyl- R^{201} or R^{200} -cycloalkyl- R^{201}

10 wherein:

R^{200} is selected from:

- $(CR^{202}R^{203})_y$ -;

- NR^{202} -;

- $NR^{202}-(CH_2)_y$ -;

15 - $(CH_2)_y-NR^{202}$ -;

-O- $(CH_2)_y$ -;

- $(CH_2)_y$ -O-;

-S-;

-O-;

20 or R^{200} represents a bond;

R^{201} represents one or more radicals selected from the group consisting of hydroxy, lower hydroxyalkyl, lower cycloalkyl; lower hydroxyalkylcarbonyl, lower cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, lower alkoxyalkylene, lower alkoxyarylene, lower carboxyalkylcarbonyl, lower alkoxyalkylcarbonyl, lower heterocyclylalkylcarbonyl, lower alkylsulfonylalkylene, amino, lower aminoalkyl, lower aralkylamino, lower alkylaminoalkylene, aminocarbonyl, lower alkylcarbonylamino, lower alkylcarbonylaminoalkylene, lower alkylaminoalkylcarbonyl, lower alkylaminoalkylcarbonylamino, lower aminoalkylcarbonylaminoalkyl, lower alkoxy carbonylamino, lower alkoxyalkylcarbonylamino, lower alkoxy carbonylaminoalkylene, lower alkylimidocarbonyl, amidino, lower alkylamidino, lower aralkylamidino, guanidino, lower guanidinoalkylene, and lower alkylsulfonylamino; and

40 R^{202} and R^{203} are independently selected from hydrido, lower alkyl, aryl and lower aralkyl; and

y is 0, 1, 2 or 3; and

1133

R⁴ is selected from aryl selected from phenyl, biphenyl, naphthyl, wherein said aryl is optionally substituted at a substitutable position with one or more radicals independently selected from halo, lower alkyl, lower alkoxy, aryloxy, lower aralkoxy, lower haloalkyl, lower alkylthio, lower alkylamino, nitro, and hydroxy; and

R⁵ is selected from hydrido, halo, amino, cyano, aminocarbonyl, lower alkyl, lower alkoxy, hydroxy, lower aminoalkyl, lower aralkyl, lower aralkyloxy, lower aralkylamino, lower alkoxycarbonyl, lower alkylamino, lower hydroxyalkylamino, lower alkylcarbonyl, lower aralkenyl, lower arylheterocyclyl, carboxy, lower cycloalkylamino, lower hydroxycycloalkylamino, lower alkoxycarbonylamino, lower alkoxyaralkylamino, lower alkylaminoalkylamino, lower heterocyclylamino, lower heterocyclylalkylamino, lower aralkylheterocyclylamino, lower alkylaminocarbonyl, lower alkylcarbonyl, lower alkoxyaralkylamino, hydrazinyl, and lower alkylhydrazinyl, or -NR⁶²R⁶³ wherein R⁶² is lower alkylcarbonyl or amino, and R⁶³ is lower alkyl or lower phenylalkyl; or

a pharmaceutically-acceptable salt or tautomer thereof.

95. A compound of Claim 94 wherein R² is R²⁰⁰-heterocyclyl-R²⁰¹.

96. A compound of Claim 94 wherein R² is R²⁰⁰-cycloalkyl-R²⁰¹.

97. A compound of Claim 94 wherein:

R¹ is selected from hydrido, methyl, ethyl, hydroxyethyl and propargyl; and

R² is R²⁰⁰-piperidinyl-R²⁰¹, R²⁰⁰-piperazinyl-R²⁰¹, or R²⁰⁰-cyclohexyl-R²⁰¹ wherein:

R²⁰⁰ is selected from:

1134

- (CR²⁰²R²⁰³)_y-;

-NR²⁰²-;

-S-;

10 -O-;

or R²⁰⁰ represents a bond;

R²⁰¹ represents one or more radicals selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-
15 1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethylene, methoxyethylene, methoxypropylene, ethoxyethylene, ethoxypropylene, propoxyethylene, propoxypropylene, methoxyphenylene, ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl,
20 cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl, chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl,
25 carboxypropylcarbonyl, methoxymethylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl,
30 methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl, methylsulfonylmethylene, amino, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino,
35 methylaminomethylene, ethylaminomethylene, methylaminoethylene, ethylaminoethylene, aminocarbonyl, methylcarbonylamino, ethylcarbonylamino, methylaminomethylcarbonyl, ethylaminomethylcarbonyl, methylcarbonylaminoethylene,
40 ethylcarbonylaminoethylene, aminomethylcarbonylaminoethylmethylene, methoxycarbonylamino, ethoxycarbonylamino,

1135

methoxymethylcarbonylamino, methoxyethylcarbonylamino,
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
45 methoxycarbonylaminomethylene,
ethoxycarbonylaminomethylene, methylimidocarbonyl,
ethylimidocarbonyl, amidino, methylamidino,
methylamidino, benzylamidino, guanidino,
guanidinomethylene, guanidinoethylene, and
50 methylsulfonylamino; and
R²⁰² and R²⁰³ are independently selected from hydrido,
methyl, ethyl, propyl, butyl, phenyl and benzyl; and
y is 0, 1 or 2; and
R⁴ is phenyl, wherein said phenyl is optionally
55 substituted with one or more radicals independently
selected from methylthio, fluoro, chloro, bromo, iodo,
methyl, ethyl, methoxy, ethoxy, phenoxy, benzyloxy,
trifluoromethyl, nitro, dimethylamino, and hydroxy; and
R⁵ is selected from hydrido, fluoro, chloro, bromo,
60 iodo, hydroxy, methyl, ethyl, propyl, benzyl,
fluorophenylethyl, fluorophenylethenyl,
fluorophenylpyrazolyl, cyano, carboxy, methoxy,
methoxycarbonyl, aminocarbonyl, acetyl, methylamino,
dimethylamino, 2-methylbutylamino, ethylamino,
65 dimethylaminoethylamino, hydroxyethylamino,
hydroxypropylamino, hydroxybutylamino,
hydroxycyclopropylamino, hydroxycyclobutylamino,
hydroxycyclopentylamino, hydroxycyclohexylamino,
imidazolylamino, morpholinylethylamino, (1-ethyl-2-
70 hydroxy)ethylamino, piperidinylamino,
pyridinylmethylamino, phenylmethylpiperidinylamino,
aminomethyl, cyclopropylamino, amino,
ethoxycarbonylamino, methoxyphenylmethylamino,
phenylmethylamino, fluorophenylmethylamino,
75 fluorophenylethylamino, methylaminoethylamino,
dimethylaminoethylamino, methylaminopropylamino,
dimethylaminopropylamino, methylaminobutylamino,
dimethylaminobutylamino, methylaminopentylamino,

1136

80 dimethylaminopentylamino, ethylaminoethylamino,
 diethylaminoethylamino, ethylaminopropylamino,
 diethylaminopropylamino, ethylaminobutylamino,
 diethylaminobutylamino, ethylaminopentylamino,
 methylaminocarbonyl, methylcarbonyl, ethylcarbonyl,
 hydrazinyl, and 1-methylhydrazinyl, or $-NR^{62}R^{63}$ wherein R^{62}
 85 is methylcarbonyl or amino, and R^{63} is methyl or benzyl;
 or

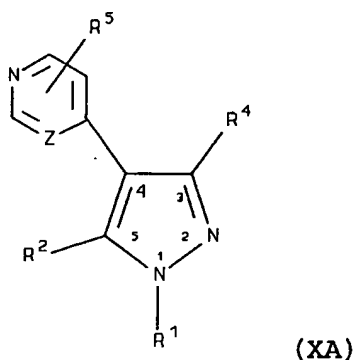
a pharmaceutically-acceptable salt or tautomer thereof.

98. A compound of Claim 97 wherein R^2 is R^{200} -piperidinyl- R^{201} .

99. A compound of Claim 97 wherein R^2 is R^{200} -pyrazinyl- R^{201} .

100. A compound of Claim 97 wherein R^2 is R^{200} -cyclohexyl- R^{201} .

101. A compound of Claim 94 having the Formula XA:



wherein:

Z represents a carbon atom or a nitrogen atom; and

5 R^1 is selected from hydrido, methyl, ethyl,

1137

hydroxyethyl and propargyl; and

R^2 is R^{200} -piperidinyl- R^{201} wherein:

R^{200} is selected from:

$-(CR^{202}R^{203})_y-$;

10 $-NR^{202}-$;

$-S-$;

$-O-$;

or R^{200} represents a bond;

R^{201} represents one or more radicals selected from

15 the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethylene, methoxyethylene, methoxypropylene, ethoxyethylene, ethoxypropylene,
20 propoxyethylene, propoxypropylene, methoxyphenylene, ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl, chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl,
25 hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxymethylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl,
30 ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl,
35 methylsulfonylmethylene, amino, aminomethyl, aminoethyl, aminopropyl, N-methylamino, N,N-dimethylamino, N-ethylamino, N,N-diethylamino, N-propylamino, N,N-dipropylamino, phenylamino, benzylamino, methylaminomethylene, ethylaminomethylene,
40 methylaminoethylene, ethylaminoethylene, aminocarbonyl, methylcarbonylamino, ethylcarbonylamino,

1138

methylaminomethylcarbonyl, ethylaminomethylcarbonyl,
methylcarbonylaminomethylene,
ethylcarbonylaminomethylene,

45 aminomethylcarbonylaminocarbonylmethylene,
methoxycarbonylamino, ethoxycarbonylamino,
methoxymethylcarbonylamino, methoxyethylcarbonylamino,
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
methoxycarbonylaminomethylene,

50 ethoxycarbonylaminomethylene, methylimidocarbonyl,
ethylimidocarbonyl, amidino, methylamidino,
methylamidino, benzylamidino, guanidino,
guanidinomethylene, guanidinoethylene, and
methylsulfonylamino; and

55 R^{202} and R^{203} are independently selected from hydrido,
methyl, ethyl, propyl, butyl, phenyl and benzyl; and
y is 0, 1 or 2; and

R^4 is phenyl, wherein said phenyl is optionally
substituted with one or more radicals independently
60 selected from fluoro, chloro, methyl, ethyl, methoxy and
ethoxy; and

R^5 is selected from hydrido, fluoro, chloro, bromo,
hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy,
methoxy, methoxycarbonyl, aminocarbonyl, acetyl,
65 methylamino, dimethylamino, 2-methylbutylamino,
ethylamino, dimethylaminoethylamino, hydroxyethylamino,
hydroxypropylamino, hydroxybutylamino,
hydroxycyclopropylamino, hydroxycyclobutylamino,
hydroxycyclopentylamino, hydroxycyclohexylamino,
70 imidazolylamino, morpholinylethylamino, (1-ethyl-2-
hydroxy)ethylamino, piperidinylamino,
pyridinylmethylamino, phenylmethylpiperidinylamino,
aminomethyl, cyclopropylamino, amino,
ethoxycarbonylamino, methoxyphenylmethylamino,
75 phenylmethylamino, fluorophenylmethylamino,
fluorophenylethylamino, methylaminoethylamino,
dimethylaminoethylamino, methylaminopropylamino,

1139

dimethylaminopropylamino, methylaminobutylamino,
dimethylaminobutylamino, methylaminopentylamino,
80 dimethylaminopentylamino, ethylaminoethylamino,
diethylaminoethylamino, ethylaminopropylamino,
diethylaminopropylamino, ethylaminobutylamino,
diethylaminobutylamino, ethylaminopentylamino,
methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl;

85 or

a pharmaceutically-acceptable salt or tautomer thereof.

102. A compound of Claim 101 wherein:

R¹ is selected from hydrido, methyl, ethyl,
hydroxyethyl and propargyl; and

R² is R²⁰⁰-piperidinyl-R²⁰¹ wherein:

5 R²⁰⁰ is selected from:

methylene;

-NR²⁰²-;

-S-;

-O-;

10 or R²⁰⁰ represents a bond;

R²⁰¹ represents one or more radicals selected from
the group consisting of hydroxy, hydroxymethyl,
hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-
dimethyl)ethyl, methoxymethyl, methoxyethyl,
15 methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl,
propoxypropyl, methoxyphenyl, ethoxyphenyl,
propoxyphenyl, hydroxymethylcarbonyl,
hydroxyethylcarbonyl, carboxymethylcarbonyl,
carboxyethylcarbonyl, methoxymethylcarbonyl,
20 methoxyethylcarbonyl, methoxypropylcarbonyl,
ethoxymethylcarbonyl, ethoxyethylcarbonyl,
ethoxypropylcarbonyl, propoxymethylcarbonyl,
propoxyethylcarbonyl, propoxypropylcarbonyl,
methoxyphenylcarbonyl, ethoxyphenylcarbonyl,
25 propoxyphenylcarbonyl, methylsulfonylmethylene, amino,

aminomethyl, aminoethyl, aminopropyl, N-benzylamino, methylaminomethylene, aminocarbonyl, methoxycarbonylamino, ethoxycarbonylamino, or methylsulfonylamino; and

30 R^{202} is selected from hydrido, methyl, ethyl, phenyl and benzyl; and

R^4 is phenyl, wherein said phenyl is optionally substituted with one or more radicals independently selected from fluoro, chloro, methyl, ethyl, methoxy and
35 ethoxy; and

R^5 is selected from hydrido, fluoro, chloro, bromo, hydroxy, methyl, ethyl, cyano, carboxy, methoxy, methoxycarbonyl, aminocarbonyl, acetyl, methylamino, dimethylamino, ethylamino, dimethylaminoethylamino,
40 hydroxyethylamino, hydroxypropylamino, hydroxybutylamino, hydroxycyclopropylamino, hydroxycyclobutylamino, hydroxycyclopentylamino, hydroxycyclohexylamino, (1-ethyl-2-hydroxy)ethylamino, aminomethyl, cyclopropylamino, amino, ethoxycarbonylamino,
45 methoxyphenylmethylamino, phenylmethylamino, fluorophenylmethylamino, fluorophenylethylamino, methylaminoethylamino, dimethylaminoethylamino, methylaminopropylamino, dimethylaminopropylamino, methylaminobutylamino, dimethylaminobutylamino,
50 methylaminopentylamino, dimethylaminopentylamino, ethylaminoethylamino, diethylaminoethylamino, ethylaminopropylamino, diethylaminopropylamino, ethylaminobutylamino, diethylaminobutylamino, ethylaminopentylamino, methylaminocarbonyl,
55 methylcarbonyl, and ethylcarbonyl; or

 a pharmaceutically-acceptable salt or tautomer thereof.

103. A compound of Claim 101 wherein:

R^1 is hydrido; and

R^2 is R^{200} -piperidinyl- R^{201} wherein:

1141

R²⁰⁰ is selected from:

- 5 methylene;
 -NR²⁰²-;
 -S-;
 -O-;
 or R²⁰⁰ represents a bond;

- 10 R²⁰¹ represents one or more radicals selected from
the group consisting of hydroxy, hydroxymethyl,
hydroxyethyl, hydroxypropyl, methoxymethyl, methoxyethyl,
methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl,
propoxypropyl, methoxyphenyl, ethoxyphenyl,
15 propoxyphenyl, hydroxymethylcarbonyl,
hydroxyethylcarbonyl, carboxymethylcarbonyl,
carboxyethylcarbonyl, methoxymethylcarbonyl,
methoxyethylcarbonyl, ethoxymethylcarbonyl,
ethoxyethylcarbonyl, methoxyphenylcarbonyl,
20 ethoxyphenylcarbonyl, amino, aminomethyl, aminoethyl,
aminopropyl, N-benzylamino, methylaminomethylene,
aminocarbonyl, methoxycarbonylamino, and
ethoxycarbonylamino; and

- R²⁰² is selected from hydrido, methyl phenyl and
25 benzyl; and

 R⁴ is phenyl, wherein said phenyl is optionally
substituted with one or more radicals independently
selected from fluoro, chloro, methyl, and methoxy; and

- R⁵ is selected from hydrido, methylamino,
30 dimethylamino, 2-methylbutylamino, ethylamino,
dimethylaminoethylamino, hydroxypropylamino,
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,
hydroxycyclopropylamino, hydroxycyclobutylamino,
hydroxycyclopentylamino, hydroxycyclohexylamino, (1-
35 ethyl-2-hydroxy)ethylamino, aminomethyl,
cyclopropylamino, amino, dimethylaminoethylamino,
dimethylaminopropylamino, dimethylaminobutylamino,
dimethylaminopentylamino, diethylaminoethylamino,
diethylaminopropylamino, diethylaminobutylamino, and

1142

- 40 diethylaminopentylamino; or
a pharmaceutically-acceptable salt or tautomer thereof.

104. A compound of Claim 101 wherein:

R^1 is hydrido; and

R^2 is R^{200} -piperidinyl- R^{201} wherein:

R^{200} is selected from:

5 methylene;

- NR^{202} -;

-S-;

-O-;

or R^{200} represents a bond;

- 10 R^{201} represents one or more radicals selected from the group consisting of methoxyethyl, methylcarbonyl, hydroxymethylcarbonyl, methoxymethylcarbonyl, and amino; and

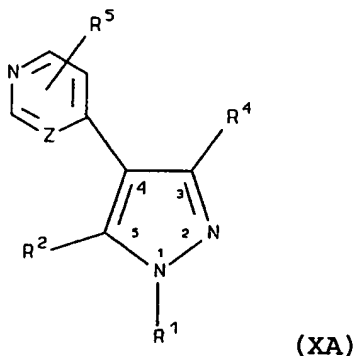
R^{202} is selected from hydrido and methyl; and

- 15 R^4 is phenyl, wherein said phenyl is optionally substituted with one or more radicals independently selected from fluoro, chloro, methyl, and methoxy; and

R^5 is selected from hydrido, hydroxypropylamino, hydroxycyclohexylamino, diethylaminoethylamino; or

- 20 a pharmaceutically-acceptable salt or tautomer thereof.

105. A compound of Claim 94 having the Formula XA:



1143

wherein:

Z represents a carbon atom or a nitrogen atom; and

5 R¹ is selected from hydrido, methyl, ethyl, hydroxyethyl and propargyl; and

R² is R²⁰⁰-piperazinyl-R²⁰¹ wherein:

R²⁰⁰ is selected from:

- (CR²⁰²R²⁰³)_y-;

10 -NR²⁰²-;

-S-;

-O-;

or R²⁰⁰ represents a bond;

R²⁰¹ represents one or more radicals selected from
15 the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethylene, methoxyethylene, methoxypropylene, ethoxyethylene, ethoxypropylene,
20 propoxyethylene, propoxypropylene, methoxyphenylene, ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl, chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl,
25 hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxymethylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl,
30 ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl,
35 methylsulfonylmethylene, amino, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino, methylaminomethylene, ethylaminomethylene, methylaminoethylene, ethylaminoethylene, aminocarbonyl,

1144

- 40 methylcarbonylamino, ethylcarbonylamino,
methylaminomethylcarbonyl, ethylaminomethylcarbonyl,
methylcarbonylaminomethylene,
ethylcarbonylaminomethylene,
aminomethylcarbonylamino, aminocarbonylmethylene,
methoxycarbonylamino, ethoxycarbonylamino,
45 methoxymethylcarbonylamino, methoxyethylcarbonylamino,
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
methoxycarbonylaminomethylene,
ethoxycarbonylaminomethylene, methylimidocarbonyl,
ethylimidocarbonyl, amidino, methylamidino,
50 methylamidino, benzylamidino, guanidino,
guanidinomethylene, guanidinoethylene, and
methylsulfonylamino; and
R²⁰² and R²⁰³ are independently selected from hydrido,
methyl, ethyl, propyl, butyl, phenyl and benzyl; and
55 y is 0, 1 or 2; and
R⁴ is phenyl, wherein said phenyl is optionally
substituted with one or more radicals independently
selected from fluoro, chloro, methyl, ethyl, methoxy and
ethoxy; and
60 R⁵ is selected from hydrido, fluoro, chloro, bromo,
hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy,
methoxy, methoxycarbonyl, aminocarbonyl, acetyl,
methylamino, dimethylamino, 2-methylbutylamino,
ethylamino, dimethylaminoethylamino, hydroxyethylamino,
65 hydroxypropylamino, hydroxybutylamino,
hydroxycyclopropylamino, hydroxycyclobutylamino,
hydroxycyclopentylamino, hydroxycyclohexylamino,
imidazolylamino, morpholinylethylamino, (1-ethyl-2-
hydroxy)ethylamino, piperidinylamino,
70 pyridinylmethylamino, phenylmethylpiperidinylamino,
aminomethyl, cyclopropylamino, amino,
ethoxycarbonylamino, methoxyphenylmethylamino,
phenylmethylamino, fluorophenylmethylamino,
fluorophenylethylamino, methylaminoethylamino,

1145

75 dimethylaminoethylamino, methylaminopropylamino,
dimethylaminopropylamino, methylaminobutylamino,
dimethylaminobutylamino, methylaminopentylamino,
dimethylaminopentylamino, ethylaminoethylamino,
diethylaminoethylamino, ethylaminopropylamino,
80 diethylaminopropylamino, ethylaminobutylamino,
diethylaminobutylamino, ethylaminopentylamino,
methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl;
or

a pharmaceutically-acceptable salt or tautomer
85 thereof.

106. A compound of Claim 105 wherein:

R^1 is selected from hydrido, methyl, ethyl,
hydroxyethyl and propargyl; and

R^2 is R^{200} -piperazinyl- R^{201} wherein:

5 R^{200} is selected from:

$-(CR^{202}R^{203})_y-$;

$-NR^{202}-$;

$-S-$;

$-O-$;

10 or R^{200} represents a bond;

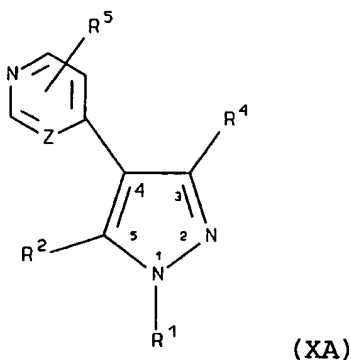
R^{201} represents one or more radicals selected from
the group consisting of hydroxy, hydroxymethyl,
hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-
dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl,
15 cyclohexyl, methoxymethylene, methoxyethylene,
ethoxyethylene, methoxyphenylene, ethoxyphenylene,
cyclopropylcarbonyl, cyclobutylcarbonyl,
cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl,
chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl,
20 hydroxyethylcarbonyl, hydroxypropylcarbonyl,
carboxymethylcarbonyl, carboxyethylcarbonyl,
carboxypropylcarbonyl, methoxymethylcarbonyl,
methoxyethylcarbonyl, methoxypropylcarbonyl,
ethoxymethylcarbonyl, ethoxyethylcarbonyl,

- 25 ethoxypropylcarbonyl, propoxymethylcarbonyl,
propoxyethylcarbonyl, propoxypropylcarbonyl,
methoxyphenylcarbonyl, ethoxyphenylcarbonyl,
propoxyphenylcarbonyl, piperidinylmethylcarbonyl,
piperazinylmethylcarbonyl, morpholinylcarbonyl,
30 methylsulfonylmethylene, amino, aminomethyl, aminoethyl,
aminopropyl, phenylamino, benzylamino,
methylaminomethylene, ethylaminomethylene,
methylaminoethylene, ethylaminoethylene, aminocarbonyl,
methylcarbonylamino, ethylcarbonylamino,
35 methylaminomethylcarbonyl, ethylaminomethylcarbonyl,
methylcarbonylaminomethylene,
ethylcarbonylaminomethylene,
aminomethylcarbonylaminoethylmethylene,
methoxycarbonylamino, ethoxycarbonylamino,
40 methoxymethylcarbonylamino, methoxyethylcarbonylamino,
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
methoxycarbonylaminomethylene,
ethoxycarbonylaminomethylene, and methylsulfonylamino;
and
- 45 R^{202} and R^{203} are independently selected from hydrido,
methyl, ethyl, phenyl and benzyl; and
y is 0, 1 or 2; and
 R^4 is phenyl, wherein said phenyl is optionally
substituted with one or more radicals independently
50 selected from fluoro, chloro, methyl, ethyl, methoxy and
ethoxy; and
 R^5 is selected from hydrido, fluoro, chloro, bromo,
hydroxy, methyl, ethyl, cyano, carboxy, methoxy,
methoxycarbonyl, aminocarbonyl, acetyl, methylamino,
55 dimethylamino, ethylamino, dimethylaminoethylamino,
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,
hydroxycyclopropylamino, hydroxycyclobutylamino,
hydroxycyclopentylamino, hydroxycyclohexylamino, (1-
ethyl-2-hydroxy)ethylamino, aminomethyl,
60 cyclopropylamino, amino, ethoxycarbonylamino,

1147

methoxyphenylmethylamino, phenylmethylamino,
 fluorophenylmethylamino, fluorophenylethylamino,
 methylaminoethylamino, dimethylaminoethylamino,
 methylaminopropylamino, dimethylaminopropylamino,
 65 methylaminobutylamino, dimethylaminobutylamino,
 methylaminopentylamino, dimethylaminopentylamino,
 ethylaminoethylamino, diethylaminoethylamino,
 ethylaminopropylamino, diethylaminopropylamino,
 ethylaminobutylamino, diethylaminobutylamino,
 70 ethylaminopentylamino, methylaminocarbonyl,
 methylcarbonyl, and ethylcarbonyl; or
 a pharmaceutically-acceptable salt or tautomer
 thereof.

107. A compound of Claim 94 having the Formula XA:



wherein:

Z represents a carbon atom or a nitrogen atom; and

5 R¹ is selected from hydrido, methyl, ethyl,
 hydroxyethyl and propargyl; and

R² is R²⁰⁰-cyclohexyl-R²⁰¹ wherein:

R²⁰⁰ is selected from:

-(CR²⁰²R²⁰³)_y-;

10 -NR²⁰²-;

-S-;

1148

-O-;

or R²⁰⁰ represents a bond;

R²⁰¹ represents one or more radicals selected from

15 the group consisting of hydroxy, hydroxymethyl,
hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-
1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl,
cyclohexyl, methoxymethylene, methoxyethylene,
methoxypropylene, ethoxyethylene, ethoxypropylene,
20 propoxyethylene, propoxypropylene, methoxyphenylene,
ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl,
cyclobutylcarbonyl, cyclopentylcarbonyl,
cyclohexylcarbonyl, benzoyl, chlorobenzoyl,
fluorobenzoyl, hydroxymethylcarbonyl,
25 hydroxyethylcarbonyl, hydroxypropylcarbonyl,
carboxymethylcarbonyl, carboxyethylcarbonyl,
carboxypropylcarbonyl, methoxymethylcarbonyl,
methoxyethylcarbonyl, methoxypropylcarbonyl,
ethoxymethylcarbonyl, ethoxyethylcarbonyl,
30 ethoxypropylcarbonyl, propoxymethylcarbonyl,
propoxyethylcarbonyl, propoxypropylcarbonyl,
methoxyphenylcarbonyl, ethoxyphenylcarbonyl,
propoxyphenylcarbonyl, piperidinylmethylcarbonyl,
piperazinylmethylcarbonyl, morpholinylcarbonyl,
35 methylsulfonylmethylene, amino, aminomethyl, aminoethyl,
aminopropyl, phenylamino, benzylamino,
methylaminomethylene, ethylaminomethylene,
methylaminoethylene, ethylaminoethylene, aminocarbonyl,
methylcarbonylamino, ethylcarbonylamino,
40 methylaminomethylcarbonyl, ethylaminomethylcarbonyl,
methylcarbonylaminomethylene,
ethylcarbonylaminomethylene,
aminomethylcarbonylaminoethylmethylene,
methoxycarbonylamino, ethoxycarbonylamino,
45 methoxymethylcarbonylamino, methoxyethylcarbonylamino,
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
methoxycarbonylaminomethylene,

1149

ethoxycarbonylaminomethylene, methylimidocarbonyl,
ethylimidocarbonyl, amidino, methylamidino,
50 methylamidino, benzylamidino, guanidino,
guanidinomethylene, guanidinoethylene, and
methylsulfonylamino; and
R²⁰² and R²⁰³ are independently selected from hydrido,
methyl, ethyl, propyl, butyl, phenyl and benzyl; and
55 y is 0, 1 or 2; and
R⁴ is phenyl, wherein said phenyl is optionally
substituted with one or more radicals independently
selected from fluoro, chloro, methyl, ethyl, methoxy and
ethoxy; and
60 R⁵ is selected from hydrido, fluoro, chloro, bromo,
hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy,
methoxy, methoxycarbonyl, aminocarbonyl, acetyl,
methylamino, dimethylamino, 2-methylbutylamino,
ethylamino, dimethylaminoethylamino, hydroxyethylamino,
65 hydroxypropylamino, hydroxybutylamino,
hydroxycyclopropylamino, hydroxycyclobutylamino,
hydroxycyclopentylamino, hydroxycyclohexylamino,
imidazolylamino, morpholinylethylamino, (1-ethyl-2-
hydroxy)ethylamino, piperidinylamino,
70 pyridinylmethylamino, phenylmethylpiperidinylamino,
aminomethyl, cyclopropylamino, amino,
ethoxycarbonylamino, methoxyphenylmethylamino,
phenylmethylamino, fluorophenylmethylamino,
fluorophenylethylamino, methylaminoethylamino,
75 dimethylaminoethylamino, methylaminopropylamino,
dimethylaminopropylamino, methylaminobutylamino,
dimethylaminobutylamino, methylaminopentylamino,
dimethylaminopentylamino, ethylaminoethylamino,
diethylaminoethylamino, ethylaminopropylamino,
80 diethylaminopropylamino, ethylaminobutylamino,
diethylaminobutylamino, ethylaminopentylamino,
methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl;
or

1150

85 a pharmaceutically-acceptable salt or tautomer thereof.

108. A compound of Claim 107 wherein:

R^1 is selected from hydrido, methyl, ethyl, hydroxyethyl and propargyl; and

R^2 is R^{200} -cyclohexyl- R^{201} wherein:

5 R^{200} is selected from:

- $(CR^{202}R^{203})_y$ -;

- NR^{202} -;

-S-;

-O-;

10 or R^{200} represents a bond;

R^{201} represents one or more radicals selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethylene, methoxyethylene, methoxypropylene, ethoxyethylene, ethoxypropylene, propoxyethylene, propoxypropylene, methoxyphenylene, ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl, chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxymethylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl, methylsulfonylmethylene, amino, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino,

15
20
25
30

1151

- methyaminomethylene, ethylaminomethylene,
35 methylaminoethylene, ethylaminoethylene, aminocarbonyl,
methylcarbonylamino, ethylcarbonylamino,
methyaminomethylcarbonyl, ethylaminomethylcarbonyl,
methylcarbonylaminomethylene,
ethylcarbonylaminomethylene,
40 aminomethylcarbonylaminoethylmethylene,
methoxycarbonylamino, ethoxycarbonylamino,
methoxymethylcarbonylamino, methoxyethylcarbonylamino,
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
methoxycarbonylaminomethylene, and
45 ethoxycarbonylaminomethylene; and
R²⁰² and R²⁰³ are independently selected from hydrido,
methyl, ethyl, phenyl and benzyl; and
y is 0, 1 or 2; and
R⁴ is phenyl, wherein said phenyl is optionally
50 substituted with one or more radicals independently
selected from fluoro, chloro, methyl, ethyl, methoxy and
ethoxy; and
R⁵ is selected from hydrido, fluoro, chloro, bromo,
hydroxy, methyl, ethyl, cyano, carboxy, methoxy,
55 methoxycarbonyl, aminocarbonyl, acetyl, methylamino,
dimethylamino, ethylamino, dimethylaminoethylamino,
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,
hydroxycyclopropylamino, hydroxycyclobutylamino,
hydroxycyclopentylamino, hydroxycyclohexylamino, (1-
60 ethyl-2-hydroxy)ethylamino, aminomethyl,
cyclopropylamino, amino, ethoxycarbonylamino,
methoxyphenylmethylamino, phenylmethylamino,
fluorophenylmethylamino, fluorophenylethylamino,
methylaminoethylamino, dimethylaminoethylamino,
65 methylaminopropylamino, dimethylaminopropylamino,
methylaminobutylamino, dimethylaminobutylamino,
methylaminopentylamino, dimethylaminopentylamino,
ethylaminoethylamino, diethylaminoethylamino,
ethylaminopropylamino, diethylaminopropylamino,

1152

- 70 ethylaminobutylamino, diethylaminobutylamino,
ethylaminopentylamino, methylaminocarbonyl,
methylcarbonyl, and ethylcarbonyl; or
a pharmaceutically-acceptable salt or tautomer
thereof.

109. A compound of Claim 107 wherein:

R¹ is hydrido; and

R² is R²⁰⁰-cyclohexyl-R²⁰¹ wherein:

R²⁰⁰ is selected from:

5 methylene;

-NR²⁰²-;

-S-;

-O-;

or R²⁰⁰ represents a bond;

- 10 R²⁰¹ represents one or more radicals selected from
the group consisting of amino, aminomethyl, aminoethyl,
aminopropyl, phenylamino, benzylamino,
methylaminomethylene, ethylaminomethylene,
methylaminoethylene, ethylaminoethylene, aminocarbonyl,
15 methylcarbonylamino, ethylcarbonylamino,
methylaminomethylcarbonyl, ethylaminomethylcarbonyl,
methylcarbonylaminomethylene,
ethylcarbonylaminomethylene,
aminomethylcarbonylaminocarbonylmethylene,
20 methoxycarbonylamino, ethoxycarbonylamino,
methoxymethylcarbonylamino, methoxyethylcarbonylamino,
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,
methoxycarbonylaminomethylene, and
ethoxycarbonylaminomethylene; and

- 25 R²⁰² is selected from hydrido, methyl, phenyl and
benzyl; and

R⁴ is phenyl, wherein said phenyl is optionally
substituted with one or more radicals independently
selected from fluoro, chloro, methyl, and methoxy; and

- 30 R⁵ is selected from hydrido, methylamino,

1153

dimethylamino, 2-methylbutylamino, ethylamino,
dimethylaminoethylamino, hydroxypropylamino,
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,
hydroxycyclopropylamino, hydroxycyclobutylamino,
35 hydroxycyclopentylamino, hydroxycyclohexylamino, (1-
ethyl-2-hydroxy)ethylamino, aminomethyl,
cyclopropylamino, amino, dimethylaminoethylamino,
dimethylaminopropylamino, dimethylaminobutylamino,
dimethylaminopentylamino, diethylaminoethylamino,
40 diethylaminopropylamino, diethylaminobutylamino, and
diethylaminopentylamino; or
a pharmaceutically-acceptable salt or tautomer
thereof.

110. A compound of Claim 94 wherein R² comprises a
substituted piperidinyl or piperazinyl moiety with at
least one substituent attached to the distal nitrogen
heteroatom or to a carbon ring atom adjacent to the
5 distal nitrogen heteroatom of the piperidine or
piperazine ring.

111. A compound Claim 94 wherein R² comprises a
substituted piperidinyl moiety with at least one
substituent attached to the distal nitrogen heteroatom or
to a carbon ring atom adjacent to the distal nitrogen
5 heteroatom of the piperidine ring.

112. A compound of Claim 94 wherein R² comprises a
substituted piperazinyl moiety with at least one
substituent attached to the distal nitrogen heteroatom or
to a carbon ring atom adjacent to the distal nitrogen
5 heteroatom of the piperazine ring.

113. A compound of Claim 94 wherein Z represents a
carbon atom.

1154

114. A compound of Claim 94 wherein Z represents a nitrogen atom.

115. A compound of Claim 94 wherein R¹ is hydrido.

116. A compound of Claim 94 wherein R²⁰⁰ represents a bond.

117. A compound of Claim 94 wherein R²⁰¹ represents one or more radicals selected from the group consisting of lower hydroxyalkyl, lower hydroxyalkylcarbonyl, and lower alkylaminoalkylene.

118. A compound of Claim 94 wherein R²⁰¹ represents one or more radicals selected from the group consisting of hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, methylaminomethylene, ethylaminomethylene, methylaminoethylene, and ethylaminoethylene.

119. A compound of Claim 94 wherein R⁴ is optionally substituted phenyl.

120. A compound of Claim 94 wherein R⁴ is phenyl optionally substituted at a substitutable position with one or more radicals independently selected from chloro, fluoro, bromo and iodo.

121. A compound of Claim 94 wherein R⁴ is phenyl optionally substituted at the meta or para position with one or more chloro radicals.

122. A compound of Claim 94 wherein R⁵ is hydrido.

1155

123. A compound of Claim 94 wherein:

R¹ is hydrido;

R²⁰⁰ represents a bond;

5 R²⁰¹ represents one or more radicals selected from
the group consisting of lower hydroxyalkyl, lower
hydroxyalkylcarbonyl, and lower alkylaminoalkylene.

R⁴ is phenyl optionally substituted at a
substitutable position with one or more radicals
independently selected from halo; and

10 R⁵ is hydrido.

124. A compound of Claim 94 wherein:

R¹ is hydrido;

R²⁰⁰ represents a bond;

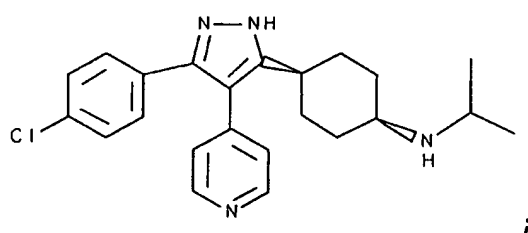
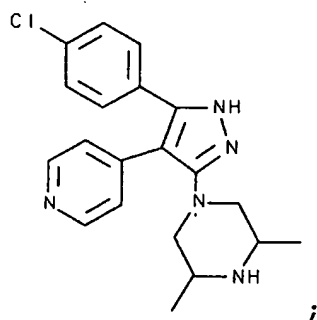
5 R²⁰¹ represents one or more radicals selected from
the group consisting of hydroxymethyl, hydroxyethyl,
hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-
dimethyl)ethyl, hydroxymethylcarbonyl,
hydroxyethylcarbonyl, hydroxypropylcarbonyl,
methylaminomethylene, ethylaminomethylene,
10 methylaminoethylene, and ethylaminoethylene;

R⁴ is phenyl optionally substituted at a
substitutable position with one or more radicals
independently selected from chloro, fluoro, bromo and
iodo; and

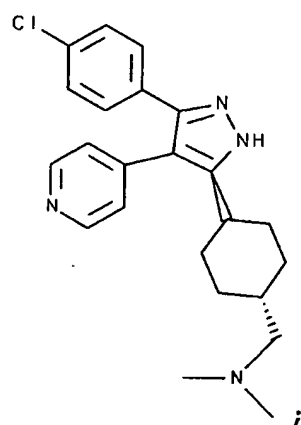
15 R⁵ is hydrido.

125. A compound selected from compounds, their
tautomers and their pharmaceutically acceptable salts, of
the group consisting of:

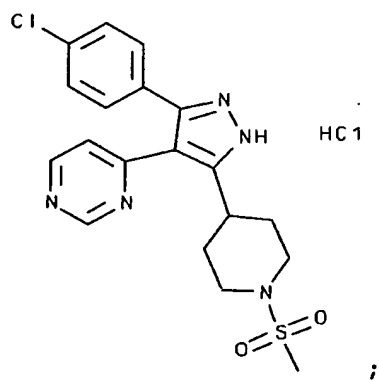
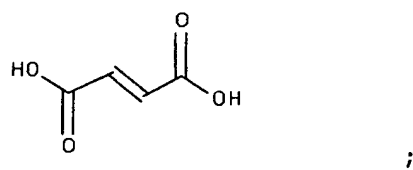
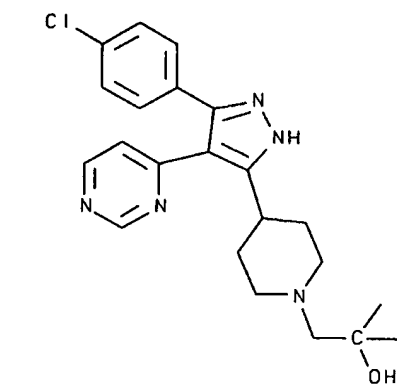
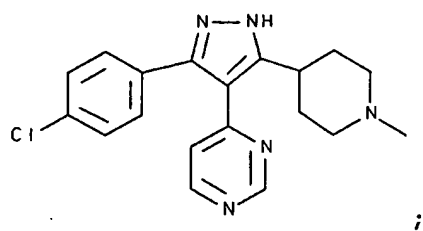
1156



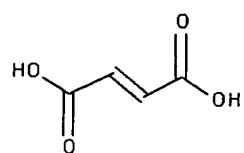
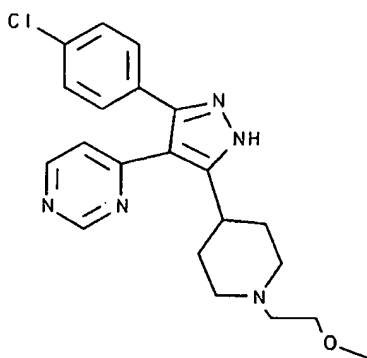
5



1157

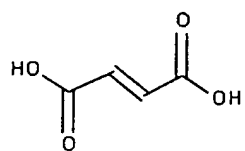
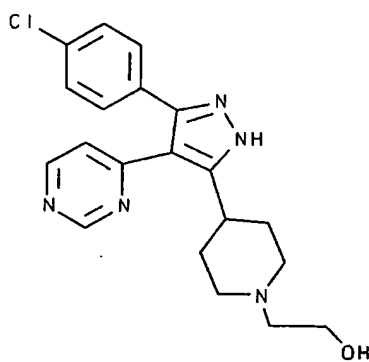


1158



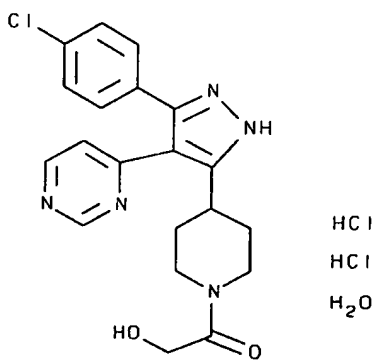
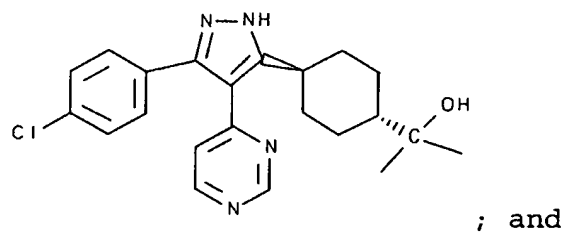
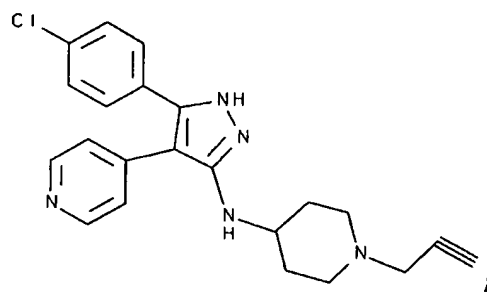
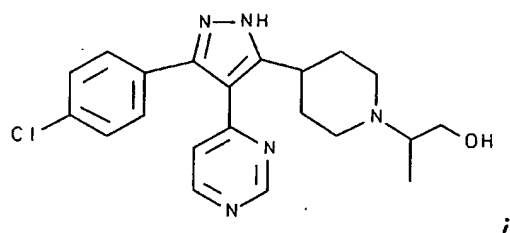
10

;



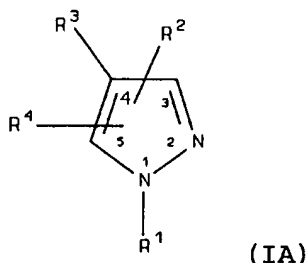
;

1159



1160

126. A compound of Formula IA



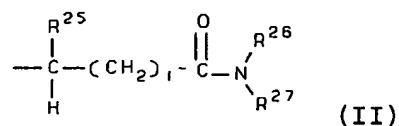
wherein

- 5 R^1 is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxyalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxyalkylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene, heterocyclylcarbonyloxyarylene,
- 10
- 15
- 20
- 25

1161

- 30 arylcarbonyloxyarylene, and
heterocyclylcarbonyloxyarylene; or

R¹ has the formula



wherein:

- 35 i is an integer from 0 to 9;
R²⁵ is selected from hydrogen, alkyl, aralkyl,
heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,
aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
alkylcarbonylalkylene, arylcarbonylalkylene, and
40 heterocyclylcarbonylaminoalkylene; and
R²⁶ is selected from hydrogen, alkyl, alkenyl,
alkynyl, cycloalkylalkylene, aralkyl,
alkoxycarbonylalkylene, and alkylaminoalkyl; and
R²⁷ is selected from alkyl, cycloalkyl, alkynyl,
45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,
cycloalkenylalkylene, cycloalkylarylene,
cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,
alkylaralkyl, aralkylarylene, alkylheterocyclyl,
alkylheterocyclylalkylene, alkylheterocyclylarylene,
50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,
alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,
aryloxyarylene, aralkoxyarylene,
alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,
alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl,
55 alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl,
alkylaminoalkylene, arylaminocarbonylalkylene,
alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,
arylaminocarbonylalkylene, alkylaminocarbonylalkylene,
arylcarbonylalkylene, alkoxycarbonylarylene,
60 aryloxycarbonylarylene, alkylaryloxycarbonylarylene,
arylcarbonylarylene, alkylarylcarbonylarylene,
alkoxycarbonylheterocyclylarylene,

alkoxycarbonylalkoxylarylene,
heterocyclylcarbonylalkylarylene, alkylthioalkylene,
65 cycloalkylthioalkylene, alkylthioarylene,
aralkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, arylsulfonylaminoalkylene,
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
70 heterocyclylalkylene, alkylheterocyclylarylene,
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
aryloxycarbonylarylene, arylcarbonylarylene,
alkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, and alkylsulfonylarylene groups
75 may be optionally substituted with one or more radicals
independently selected from alkyl, halo, haloalkyl,
alkoxy, keto, amino, nitro, and cyano; or

R^{27} is $-CHR^{28}R^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
is selected from aralkyl, aralkoxyalkylene,
80 heterocyclylalkylene, alkylheterocyclylalkylene,
alkoxycarbonylalkylene, alkylthioalkylene, and
aralkylthioalkylene; wherein said aralkyl and
heterocyclyl groups may be optionally substituted with
one or more radicals independently selected from alkyl
85 and nitro; or

R^{26} and R^{27} together with the nitrogen atom to which
they are attached form a heterocycle, wherein said
heterocycle is optionally substituted with one or more
radicals independently selected from alkyl, aryl,
90 heterocyclyl, heterocyclylalkylene,
alkylheterocyclylalkylene, aryloxyalkylene,
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
alkoxycarbonylamino; wherein said aryl,
95 heterocyclylalkylene and aryloxyalkylene radicals may be
optionally substituted with one or more radicals
independently selected from halogen, alkyl and alkoxy;
and

1163

R^2 is R^{200} -cycloalkyl- R^{201} wherein:

100 R^{200} is selected from:

- $(CR^{202}R^{203})_y-$;

- $C(O)-$;

- $C(O)-(CH_2)_y-$;

- $C(O)-O-(CH_2)_y-$;

105 - $(CH_2)_y-C(O)-$;

- $O-(CH_2)_y-C(O)-$;

- $NR^{202}-$;

- $NR^{202}-(CH_2)_y-$;

- $(CH_2)_y-NR^{202}-$;

110 - $(CH_2)_y-NR^{202}-(CH_2)_z-$;

- $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;

- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;

- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;

- $S(O)_x-(CR^{202}R^{203})_y-$;

115 - $(CR^{202}R^{203})_y-S(O)_x-$;

- $S(O)_x-(CR^{202}R^{203})_y-O-$;

- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$;

- $O-(CH_2)_y-$;

- $(CH_2)_y-O-$;

120 - $S-$; and

- $O-$;

R^{201} represents one or more radicals selected from the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl, alkylamino, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,

1164

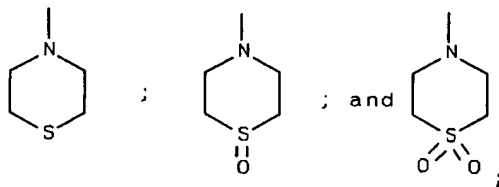
135 alkylaminoalkylcarbonylamino,
 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,
 alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene,
 alkylimidocarbonyl, amidino, alkylamidino,
 aralkylamidino, guanidino, guanidinoalkylene, and
 140 alkylsulfonylamino; and

R^{202} and R^{203} are independently selected from hydrido,
 alkyl, aryl and aralkyl; and

y and z are independently 0, 1, 2, 3, 4, 5 or 6
 wherein y + z is less than or equal to 6; and

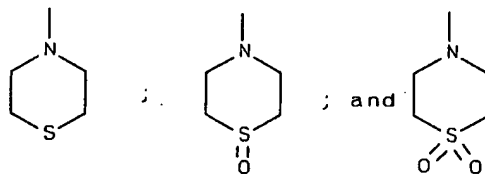
145 x is 0, 1 or 2; and

R^3 is selected from pyridinyl, pyrimidinyl,
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,
 thiazolylalkyl, thiazolylamino,



150

wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl,
 purinyl, maleimidyl, pyridonyl, thiazolyl,
 thiazolylalkyl, thiazolylamino,



155

groups may be optionally substituted with one or more
 radicals independently selected from halo, keto, alkyl,
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,
 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,
 160 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,
 alkenylamino, alkynylamino, cycloalkylamino,
 cycloalkenylamino, arylamino, haloaryl amino,
 heterocyclylamino, aminocarbonyl, cyano, hydroxy,

1165

165 hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,
aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,
alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl,
alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,
aminosulfinyl, aminosulfonyl, alkylsulfonylamino,
170 alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,
aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,
alkylheterocyclylamino, heterocyclylalkylamino,
alkylheterocyclylalkylamino, aralkylheterocyclylamino,
heterocyclylheterocyclylalkylamino,
175 alkoxycarbonylheterocyclylamino, nitro,
alkylaminocarbonyl, alkylcarbonylamino,
haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,
hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$
wherein R^{44} is alkylcarbonyl or amino, and R^{45} is alkyl or
180 aralkyl; and

R^4 is selected from hydrido, alkyl, alkenyl, alkynyl,
cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
 R^4 is optionally substituted with one or more radicals
independently selected from halo, alkyl, alkenyl,
185 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,
alkylthioalkylene, arylthioalkylene, alkylsulfinyl,
alkylsulfinylalkylene, arylsulfinylalkylene,
alkylsulfonyl, alkylsulfonylalkylene,
arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
190 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
nitro, alkylamino, arylamino, alkylaminoalkylene,
arylaminoalkylene, aminoalkylamino, and hydroxy;

provided R^3 is not 2-pyridinyl when R^4 is a phenyl
195 ring containing a 2-hydroxy substituent and when R^1 is
hydrido; and

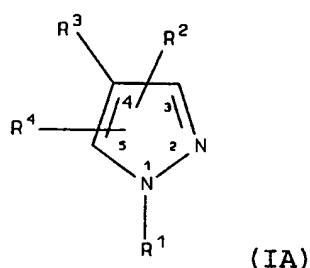
further provided that R^4 is not methylsulfonylphenyl
or aminosulfonylphenyl; and

further provided that R^1 is not methylsulfonylphenyl;
200 or

1166

a pharmaceutically-acceptable salt or tautomer thereof.

127. A compound of Formula IA



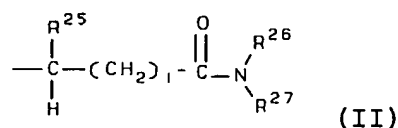
wherein

- 5 R^1 is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxy carbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxy carbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene,
- 10
- 15
- 20
- 25

1167

alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 30 arylcarbonyloxyarylene, and
 heterocyclylcarbonyloxyarylene; or

R¹ has the formula



wherein:

35 i is an integer from 0 to 9;

R²⁵ is selected from hydrogen, alkyl, aralkyl,
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
 alkylcarbonylalkylene, arylcarbonylalkylene, and
 40 heterocyclylcarbonylaminoalkylene; and

R²⁶ is selected from hydrogen, alkyl, alkenyl,
 alkynyl, cycloalkylalkylene, aralkyl,
 alkoxy carbonylalkylene, and alkylaminoalkyl; and

R²⁷ is selected from alkyl, cycloalkyl, alkynyl,
 45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,
 cycloalkenylalkylene, cycloalkylarylene,
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,
 alkylheterocyclylalkylene, alkylheterocyclylarylene,
 50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,
 alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,
 aryloxyarylene, aralkoxyarylene,
 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,
 alkoxy carbonylalkylene, alkoxy carbonyl heterocyclyl,
 55 alkoxy carbonyl heterocyclyl carbonylalkylene, aminoalkyl,
 alkylaminoalkylene, arylaminocarbonylalkylene,
 alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,
 arylaminocarbonylalkylene, alkylaminocarbonylalkylene,
 arylcarbonylalkylene, alkoxy carbonylarylene,
 60 aryloxy carbonylarylene, alkylaryloxy carbonylarylene,

1168

arylcarbonylarylene, alkylarylcarbonylarylene,
alkoxycarbonylheterocyclylarylene,
alkoxycarbonylalkoxylarylene,
heterocyclylcarbonylalkylarylene, alkylthioalkylene,
65 cycloalkylthioalkylene, alkylthioarylene,
aralkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, arylsulfonylaminoalkylene,
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
70 heterocyclylalkylene, alkylheterocyclylarylene,
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
aryloxycarbonylarylene, arylcarbonylarylene,
alkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, and alkylsulfonylarylene groups
75 may be optionally substituted with one or more radicals
independently selected from alkyl, halo, haloalkyl,
alkoxy, keto, amino, nitro, and cyano; or

R^{27} is $-CHR^{28}R^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
is selected from aralkyl, aralkoxyalkylene,
80 heterocyclylalkylene, alkylheterocyclylalkylene,
alkoxycarbonylalkylene, alkylthioalkylene, and
aralkylthioalkylene; wherein said aralkyl and
heterocyclyl groups may be optionally substituted with
one or more radicals independently selected from alkyl
85 and nitro; or

R^{26} and R^{27} together with the nitrogen atom to which
they are attached form a heterocycle, wherein said
heterocycle is optionally substituted with one or more
radicals independently selected from alkyl, aryl,
90 heterocyclyl, heterocyclylalkylene,
alkylheterocyclylalkylene, aryloxyalkylene,
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
alkoxycarbonylamino; wherein said aryl,
95 heterocyclylalkylene and aryloxyalkylene radicals may be
optionally substituted with one or more radicals

1169

independently selected from halogen, alkyl and alkoxy;
and

R^2 is R^{200} -aryl- R^{201} wherein:

100 R^{200} is selected from:

- $(CR^{202}R^{203})_y-$;

- $C(O)-$;

- $C(O)-(CH_2)_y-$;

- $C(O)-O-(CH_2)_y-$;

105 - $(CH_2)_y-C(O)-$;

- $O-(CH_2)_y-C(O)-$;

- $NR^{202}-$;

- $NR^{202}-(CH_2)_y-$;

- $(CH_2)_y-NR^{300}-$;

110 - $(CH_2)_y-NR^{202}-(CH_2)_{z1}-$;

- $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;

- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;

- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;

- $S(O)_x-(CR^{202}R^{203})_y-$;

115 - $(CR^{202}R^{203})_y-S(O)_x-$;

- $S(O)_x-(CR^{202}R^{203})_y-O-$;

- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$;

- $O-(CH_2)_y-$;

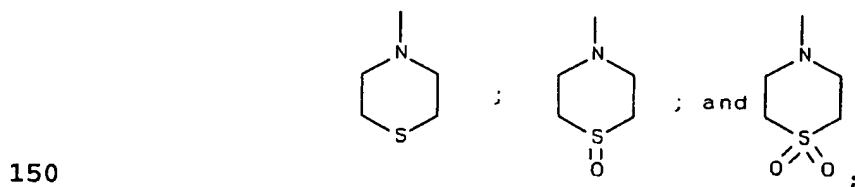
- $(CH_2)_y-O-$; and

120 - $O-$;

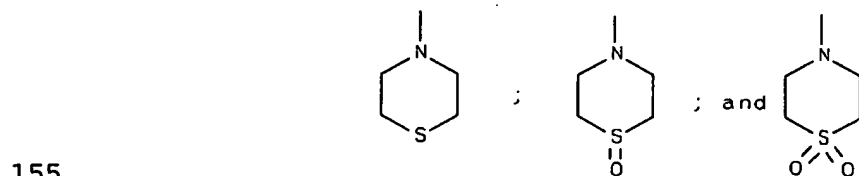
R^{201} represents one or more radicals selected from the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl, alkylamino, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino,

1170

- alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,
 alkylaminoalkylcarbonylamino,
 135 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,
 alkoxylalkylcarbonylamino, alkoxycarbonylaminoalkylene,
 alkylimidocarbonyl, amidino, alkylamidino,
 aralkylamidino, guanidino, guanidinoalkylene, and
 alkylsulfonylamino; and
 140 R^{202} and R^{203} are independently selected from hydrido,
 alkyl, aryl and aralkyl; and
 R^{300} is selected from alkyl, aryl and aralkyl; and
 y and z are independently 0, 1, 2, 3, 4, 5 or 6
 wherein y + z; and y1 is 1, 2, 3, 4, 5 or 6; wherein y +
 145 z and y1 + z are less than or equal to 6; and
 x is 0, 1 or 2; and
 R^3 is selected from pyridinyl, pyrimidinyl,
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,
 thiazolylalkyl, thiazolylamino,



wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl,
 purinyl, maleimidyl, pyridonyl, thiazolyl,
 thiazolylalkyl, thiazolylamino,



- groups may be optionally substituted with one or more
 radicals independently selected from halo, keto, alkyl,
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,
 160 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,
 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,

1171

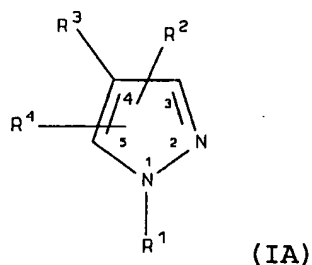
165 alkenylamino, alkynylamino, cycloalkylamino,
cycloalkenylamino, arylamino, haloarylamino,
heterocyclylamino, aminocarbonyl, cyano, hydroxy,
hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,
aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,
alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl,
alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,
170 aminosulfinyl, aminosulfonyl, alkylsulfonylamino,
alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,
aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,
alkylheterocyclylamino, heterocyclylalkylamino,
alkylheterocyclylalkylamino, aralkylheterocyclylamino,
175 heterocyclylheterocyclylalkylamino,
alkoxycarbonylheterocyclylamino, nitro,
alkylaminocarbonyl, alkylcarbonylamino,
haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,
hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$
180 wherein R^{44} is alkylcarbonyl or amino, and R^{45} is alkyl or
aralkyl; and

R^4 is selected from hydrido, alkyl, alkenyl, alkynyl,
cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
 R^4 is optionally substituted with one or more radicals
185 independently selected from halo, alkyl, alkenyl,
alkynyl, aryl, heterocyclyl, alkylthio, arylthio,
alkylthioalkylene, arylthioalkylene, alkylsulfinyl,
alkylsulfinylalkylene, arylsulfinylalkylene,
alkylsulfonyl, alkylsulfonylalkylene,
190 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
nitro, alkylamino, arylamino, alkylaminoalkylene,
arylaminoalkylene, aminoalkylamino, and hydroxy;
195 provided R^3 is not 2-pyridinyl when R^4 is a phenyl
ring containing a 2-hydroxy substituent and when R^1 is
hydrido; and
further provided that R^4 is not methylsulfonylphenyl

1172

or aminosulfonylphenyl; and
 200 further provided that R¹ is not methylsulfonylphenyl;
 or
 a pharmaceutically-acceptable salt or tautomer
 thereof.

128. A compound of Formula IA



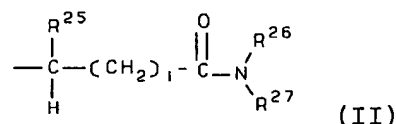
wherein

5 R¹ is selected from hydrido, hydroxy, alkyl,
 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl,
 heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene,
 heterocyclylalkylene, haloalkyl, haloalkenyl,
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,
 10 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,
 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl,
 heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl,
 alkylthioalkylene, alkenylthioalkylene,
 15 alkylthioalkenylene, amino, aminoalkyl, alkylamino,
 alkenylamino, alkynylamino, arylamino, heterocyclylamino,
 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,
 arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
 20 heterocyclylsulfonyl, alkylaminoalkylene,
 alkylsulfonylalkylene, acyl, acyloxycarbonyl,
 alkoxy carbonylalkylene, aryloxycarbonylalkylene,
 heterocycliloxy carbonylalkylene, alkoxy carbonylaryl,
 aryloxycarbonylaryl, heterocycliloxy carbonylaryl,

1173

- 25 alkylcarbonylalkylene, arylcarbonylalkylene,
 heterocyclylcarbonylalkylene, alkylcarbonylarylene,
 arylcarbonylarylene, heterocyclylcarbonylarylene,
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 30 arylcarbonyloxyarylene, and
 heterocyclylcarbonyloxyarylene; or

R^1 has the formula



wherein:

- 35 i is an integer from 0 to 9;
 R^{25} is selected from hydrogen, alkyl, aralkyl,
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
 alkylcarbonylalkylene, arylcarbonylalkylene, and
 40 heterocyclylcarbonylaminoalkylene; and
 R^{26} is selected from hydrogen, alkyl, alkenyl,
 alkynyl, cycloalkylalkylene, aralkyl,
 alkoxyalkylene, and alkylaminoalkyl; and
 R^{27} is selected from alkyl, cycloalkyl, alkynyl,
 45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,
 cycloalkenylalkylene, cycloalkylarylene,
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,
 alkylheterocyclylalkylene, alkylheterocyclylarylene,
 50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,
 alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,
 aryloxyarylene, aralkoxyarylene,
 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,
 alkoxyalkoxyalkylene, alkoxyalkoxyheterocyclyl,
 55 alkoxyalkoxyheterocyclylalkylene, aminoalkyl,
 alkylaminoalkylene, arylaminocarbonylalkylene,
 alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,

1174

arylaminocarbonylalkylene, alkylaminocarbonylalkylene,
 arylcarbonylalkylene, alkoxycarbonylarylene,
 60 aryloxy carbonylarylene, alkylaryloxy carbonylarylene,
 arylcarbonylarylene, alkylarylcarbonylarylene,
 alkoxycarbonyl heterocyclylarylene,
 alkoxycarbonylalkoxyarylene,
 heterocyclylcarbonylalkylarylene, alkylthioalkylene,
 65 cycloalkylthioalkylene, alkylthioarylene,
 aralkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, arylsulfonylaminoalkylene,
 alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
 said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
 70 heterocyclylalkylene, alkylheterocyclylarylene,
 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
 aryloxy carbonylarylene, arylcarbonylarylene,
 alkylthioarylene, heterocyclylthioarylene,
 arylthioalkylarylene, and alkylsulfonylarylene groups
 75 may be optionally substituted with one or more radicals
 independently selected from alkyl, halo, haloalkyl,
 alkoxy, keto, amino, nitro, and cyano; or

R^{27} is $-CHR^{28}R^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
 is selected from aralkyl, aralkoxyalkylene,
 80 heterocyclylalkylene, alkylheterocyclylalkylene,
 alkoxycarbonylalkylene, alkylthioalkylene, and
 aralkylthioalkylene; wherein said aralkyl and
 heterocyclyl groups may be optionally substituted with
 one or more radicals independently selected from alkyl
 85 and nitro; or

R^{26} and R^{27} together with the nitrogen atom to which
 they are attached form a heterocycle, wherein said
 heterocycle is optionally substituted with one or more
 radicals independently selected from alkyl, aryl,
 90 heterocyclyl, heterocyclylalkylene,
 alkylheterocyclylalkylene, aryloxyalkylene,
 alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
 alkoxycarbonyl, aralkoxycarbonyl, alkylamino and

1175

alkoxycarbonylamino; wherein said aryl,
 95 heterocyclylalkylene and aryloxyalkylene radicals may be
 optionally substituted with one or more radicals
 independently selected from halogen, alkyl and alkoxy;
 and

R^2 is R^{200} -heterocyclyl- R^{201} wherein:

100 R^{200} is selected from:

- $(CR^{301}R^{302})_y-$;
 - $C(O)-(CH_2)_{y1}-$;
 - $C(O)-O-(CH_2)_y-$;
 - $(CH_2)_y-C(O)-$;
 105 - $O-(CH_2)_y-C(O)-$;
 - $NR^{303}-$;
 - $NR^{303}-(CH_2)_y-$;
 - $(CH_2)_{y1}-NR^{202}-$;
 - $(CH_2)_y-NR^{202}-(CH_2)_{z1}-$;
 110 - $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;
 - $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;
 - $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;
 - $S(O)_x-(CR^{202}R^{203})_y-$;
 - $(CR^{202}R^{203})_y-S(O)_x-$;
 115 - $S(O)_x-(CR^{202}R^{203})_y-O-$;
 - $S(O)_x-(CR^{202}R^{203})_y-C(O)-$;
 - $O-(CH_2)_y-$; and
 - $(CH_2)_y-O-$;

R^{201} represents one or more radicals selected from
 120 the group consisting of hydrido, halogen, hydroxy,
 carboxy, keto, alkyl, hydroxyalkyl, haloalkyl,
 cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl,
 aralkyl, heterocyclylalkylene, alkylcarbonyl,
 hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl,
 125 haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene,
 alkoxycarbonyl, carboxyalkylcarbonyl,
 alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl,
 alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,
 alkylamino, aralkylamino, alkylaminoalkylene,

1176

- 130 aminocarbonyl, alkylcarbonylamino,
 alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,
 alkylaminoalkylcarbonylamino,
 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,
 alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene,
 135 alkylimidocarbonyl, amidino, alkylamidino,
 aralkylamidino, guanidino, guanidinoalkylene, and
 alkylsulfonylamino; and

R^{202} and R^{203} are independently selected from hydrido,
 alkyl, aryl and aralkyl; and

- 140 R^{301} and R^{302} are independently selected from aryl and
 aralkyl; and

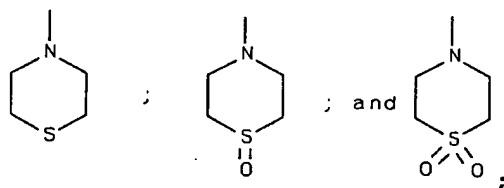
R^{303} is selected from alkyl, aryl and aralkyl; and

y and z are independently 0, 1, 2, 3, 4, 5 or 6; and
 y1 is 1, 2, 3, 4, 5 or 6; wherein y + z and y1 + z are

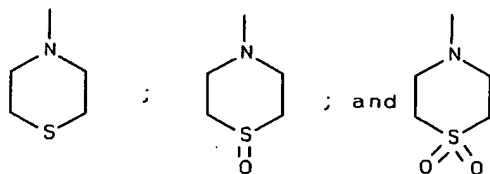
- 145 less than or equal to 6; and

x is 0, 1 or 2; wherein either x or y is other than
 0 when R^{200} is $-S(O)_x-(CR^{202}R^{203})_y-$; and

- R^3 is selected from pyridinyl, pyrimidinyl,
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,
 150 thiazolylalkyl, thiazolylamino,



- wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl,
 purinyl, maleimidyl, pyridonyl, thiazolyl,
 155 thiazolylalkyl, thiazolylamino,



groups may be optionally substituted with one or more
 radicals independently selected from halo, keto, alkyl,

1177

- 160 aralkyl, aralkenyl, arylheterocyclyl, carboxy,
carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,
alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,
aralkoxy, heterocyclylalkoxy, amino, alkylamino,
alkenylamino, alkynylamino, cycloalkylamino,
165 cycloalkenylamino, arylamino, haloaryl amino, heterocyclylamino, aminocarbonyl, cyano, hydroxy,
hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,
aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,
alkoxycarbonyl, aryloxycarbonyl, heterocyclylloxycarbonyl,
170 alkoxycarbonylamino, alkoxyaryl amino, alkoxyaralkyl amino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino,
alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,
aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,
alkylheterocyclylamino, heterocyclylalkylamino,
175 alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino,
alkoxycarbonylheterocyclylamino, nitro,
alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,
180 hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and -NR⁴⁴R⁴⁵ wherein R⁴⁴ is alkylcarbonyl or amino, and R⁴⁵ is alkyl or aralkyl; and
R⁴ is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
185 R⁴ is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl, alkylsulfinylalkylene, arylsulfinylalkylene,
190 alkylsulfonyl, alkylsulfonylalkylene, arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkylene,
195 arylaminoalkylene, aminoalkylamino, and hydroxy;

1178

provided R³ is not 2-pyridinyl when R⁴ is a phenyl ring containing a 2-hydroxy substituent and when R¹ is hydrido; and

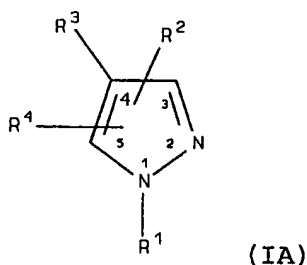
200 further provided R² is selected from aryl, heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl when R⁴ is hydrido; and

further provided that R⁴ is not methylsulfonylphenyl or aminosulfonylphenyl; and

205 or further provided that R¹ is not methylsulfonylphenyl;

a pharmaceutically-acceptable salt or tautomer thereof.

129. A compound of Formula IA



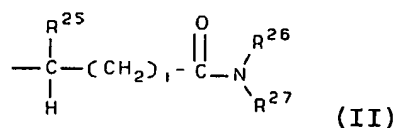
wherein

5 R¹ is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, 10 alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,

1179

arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,
 20 heterocyclylsulfonyl, alkylaminoalkylene,
 alkylsulfonylalkylene, acyl, acyloxycarbonyl,
 alkoxycarbonylalkylene, aryloxycarbonylalkylene,
 heterocyclylloxycarbonylalkylene, alkoxycarbonylarylene,
 aryloxycarbonylarylene, heterocyclylloxycarbonylarylene,
 25 alkylcarbonylalkylene, arylcarbonylalkylene,
 heterocyclylcarbonylalkylene, alkylcarbonylarylene,
 arylcarbonylarylene, heterocyclylcarbonylarylene,
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,
 30 arylcarbonyloxyarylene, and
 heterocyclylcarbonyloxyarylene; or

R^1 has the formula



wherein:

35 i is an integer from 0 to 9;

R^{25} is selected from hydrogen, alkyl, aralkyl,
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
 alkylcarbonylalkylene, arylcarbonylalkylene, and
 40 heterocyclylcarbonylaminoalkylene; and

R^{26} is selected from hydrogen, alkyl, alkenyl,
 alkynyl, cycloalkylalkylene, aralkyl,
 alkoxycarbonylalkylene, and alkylaminoalkyl; and

R^{27} is selected from alkyl, cycloalkyl, alkynyl,
 45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,
 cycloalkenylalkylene, cycloalkylarylene,
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,
 alkylheterocyclylalkylene, alkylheterocyclylarylene,
 50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,

1180

alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,
aryloxyarylene, aralkoxyarylene,
alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,
alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl,
55 alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl,
alkylaminoalkylene, arylaminocarbonylalkylene,
alkoxyarylaminoalkylene, aminocarbonylalkylene,
arylaminocarbonylalkylene, alkylaminocarbonylalkylene,
arylcarbonylalkylene, alkoxycarbonylarylene,
60 aryloxycarbonylarylene, alkylaryloxycarbonylarylene,
arylcarbonylarylene, alkylarylcarbonylarylene,
alkoxycarbonylheterocyclylarylene,
alkoxycarbonylalkoxyarylene,
heterocyclylcarbonylalkylarylene, alkylthioalkylene,
65 cycloalkylthioalkylene, alkylthioarylene,
aralkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, arylsulfonylaminoalkylene,
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
70 heterocyclylalkylene, alkylheterocyclylarylene,
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
aryloxycarbonylarylene, arylcarbonylarylene,
alkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, and alkylsulfonylarylene groups
75 may be optionally substituted with one or more radicals
independently selected from alkyl, halo, haloalkyl,
alkoxy, keto, amino, nitro, and cyano; or

R^{27} is $-CHR^{28}R^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
is selected from aralkyl, aralkoxyalkylene,
80 heterocyclylalkylene, alkylheterocyclylalkylene,
alkoxycarbonylalkylene, alkylthioalkylene, and
aralkylthioalkylene; wherein said aralkyl and
heterocyclyl groups may be optionally substituted with
one or more radicals independently selected from alkyl
85 and nitro; or

R^{26} and R^{27} together with the nitrogen atom to which

1181

they are attached form a heterocycle, wherein said heterocycle is optionally substituted with one or more radicals independently selected from alkyl, aryl, 90 heterocyclyl, heterocyclylalkylene, alkylheterocyclylalkylene, aryloxyalkylene, alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl, alkoxycarbonyl, aralkoxycarbonyl, alkylamino and alkoxycarbonylamino; wherein said aryl, 95 heterocyclylalkylene and aryloxyalkylene radicals may be optionally substituted with one or more radicals independently selected from halogen, alkyl and alkoxy; and

R^2 is selected from hydrido, halogen, mercapto, 100 alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxyalkyl, aralkyl, alkylheterocyclyl, heterocyclylalkyl, heterocyclylheterocyclyl, heterocyclylalkylheterocyclyl, alkylamino, alkenylamino, alkynylamino, arylamino, aryl(hydroxyalkyl)amino, 105 heterocyclylamino, heterocyclylalkylamino, aralkylamino, N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl, aminoalkylamino, aminocarbonylalkylene, arylaminoalkylene, alkylaminoalkylene, arylaminoarylene, alkylaminoarylene, alkylaminoalkylamino, 110 alkylcarbonylaminoalkylene, aminoalkylcarbonylaminoalkylene, alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl, aminoalkylthio, alkylaminocarbonylalkylthio, alkylaminoalkylaminocarbonylalkylthio, alkoxy, 115 heterocycliloxy, alkylthio, cyanoalkylthio, alkenylthio, alkynylthio, carboxyalkylthio, arylthio, heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl, alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl, alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl, 120 carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl, alkoxycarbonylalkyl, alkoxycarbonylalkylamino, alkoxycarbonylheterocyclyl,

1182

alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,
 alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,
 125 alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl,
 aralkythio, heterocyclylalkylthio, aminoalkoxy,
 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,
 alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; wherein
 the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and
 130 cycloalkenyl groups may be optionally substituted with
 one or more radicals independently selected from halo,
 keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl,
 aralkyl, heterocyclylalkyl, epoxyalkyl,
 amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy,
 135 haloalkyl, alkylamino, alkynylamino,
 alkylaminoalkylamino, heterocyclylalkylamino,
 alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,
 arylsulfonyl, and aralkylsulfonyl; or

R^2 is R^{200} -heterocyclyl- R^{201} , R^{200} -aryl- R^{201} , or R^{200} -
 140 cycloalkyl- R^{201} wherein:

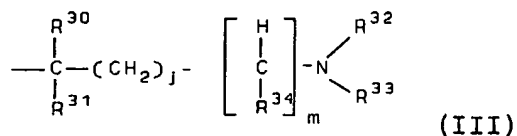
R^{200} is selected from:

- $(CR^{202}R^{203})_y-$;
- $C(O)-$;
- $C(O)-(CH_2)_y-$;
- 145 - $C(O)-O-(CH_2)_y-$;
- $(CH_2)_y-C(O)-$;
- $O-(CH_2)_y-C(O)-$;
- $NR^{202}-$;
- $NR^{202}-(CH_2)_y-$;
- 150 - $(CH_2)_y-NR^{202}-$;
- $(CH_2)_y-NR^{202}-(CH_2)_z-$;
- $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;
- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;
- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;
- 155 - $S(O)_x-(CR^{202}R^{203})_y-$;
- $(CR^{202}R^{203})_y-S(O)_x-$;
- $S(O)_x-(CR^{202}R^{203})_y-O-$;
- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$;

1183

- O-(CH₂)_y-;
 160 - (CH₂)_y-O-;
 -S-;
 -O-;
 or R²⁰⁰ represents a bond;
 R²⁰¹ represents one or more radicals selected from
 165 the group consisting of hydrido, halogen, hydroxy,
 carboxy, keto, alkyl, hydroxyalkyl, haloalkyl,
 cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl,
 aralkyl, heterocyclylalkylene, alkylcarbonyl,
 hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl,
 170 haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene,
 alkoxycarbonyl, carboxyalkylcarbonyl,
 alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl,
 alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,
 alkylamino, aralkylamino, alkylaminoalkylene,
 175 aminocarbonyl, alkylcarbonylamino,
 alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,
 alkylaminoalkylcarbonylamino,
 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,
 alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene,
 180 alkylimidocarbonyl, amidino, alkylamidino,
 aralkylamidino, guanidino, guanidinoalkylene, and
 alkylsulfonylamino; and
 R²⁰² and R²⁰³ are independently selected from hydrido,
 alkyl, aryl and aralkyl; and
 185 y and z are independently 0, 1, 2, 3, 4, 5 or 6
 wherein y + z is less than or equal to 6; and
 x is 0, 1 or 2; or
 R² is -NHCR²⁰⁴R²⁰⁵ wherein R²⁰⁴ is alkylaminoalkylene,
 and R²⁰⁵ is aryl; or
 190 R² is -C(NR²⁰⁶)R²⁰⁷ wherein R²⁰⁶ is selected from
 hydrogen and hydroxy, and R²⁰⁷ is selected from alkyl,
 aryl and aralkyl; or
 R² has the formula:

1184



195 wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

200 R³⁰ and R³¹ are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

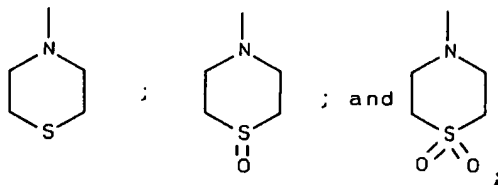
205 R³² is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene;

210 R³³ is selected from hydrogen, alkyl, -C(O)R³⁵, -C(O)OR³⁵, -SO₂R³⁶, -C(O)NR³⁷R³⁸, and -SO₂NR³⁹R⁴⁰, wherein R³⁵, R³⁶, R³⁷, R³⁸, R³⁹ and R⁴⁰ are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

R³⁴ is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or

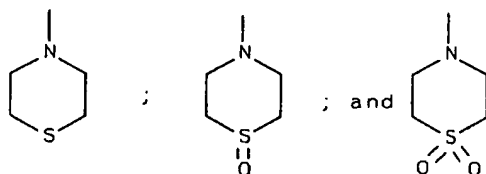
215 R² is -CR⁴¹R⁴² wherein R⁴¹ is aryl, and R⁴² is hydroxy; and

R³ is selected from maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



220 wherein the R³ maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,

1185

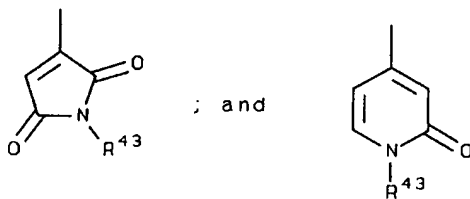


groups may be optionally substituted with one or more
 225 radicals independently selected from halo, keto, alkyl,
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,
 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,
 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,
 230 alkenylamino, alkynylamino, cycloalkylamino,
 cycloalkenylamino, arylamino, haloaryl amino,
 heterocyclylamino, aminocarbonyl, cyano, hydroxy,
 hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,
 aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,
 235 alkoxycarbonyl, aryloxycarbonyl, heterocyclylloxycarbonyl,
 alkoxycarbonylamino, alkoxyaryl amino, alkoxyaralkylamino,
 aminosulfinyl, aminosulfonyl, alkylsulfonylamino,
 alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,
 aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,
 240 alkylheterocyclylamino, heterocyclylalkylamino,
 alkylheterocyclylalkylamino, aralkylheterocyclylamino,
 heterocyclylheterocyclylalkylamino,
 alkoxycarbonylheterocyclylamino, nitro,
 alkylaminocarbonyl, alkylcarbonylamino,
 245 haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,
 hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$
 wherein R^{44} is alkylcarbonyl or amino, and R^{45} is alkyl or
 aralkyl; and

R^4 is selected from hydrido, alkyl, alkenyl, alkynyl,
 250 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
 R^4 is optionally substituted with one or more radicals
 independently selected from halo, alkyl, alkenyl,
 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,
 alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

1186

- 255 alkylsulfinylalkylene, arylsulfinylalkylene,
 alkylsulfonyl, alkylsulfonylalkylene,
 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
 260 nitro, alkylamino, arylamino, alkylaminoalkylene,
 arylaminoalkylene, aminoalkylamino, and hydroxy;
 provided R^3 is not



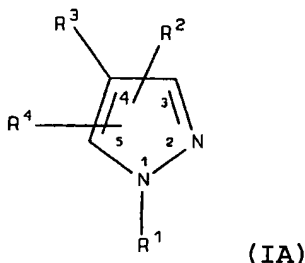
(IV)

(V)

- 265 wherein R^{43} is selected from hydrogen, alkyl,
 aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;
 and
 further provided R^2 is selected from aryl,
 heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl
 270 when R^4 is hydrido; and
 further provided that R^4 is not methylsulfonylphenyl
 or aminosulfonylphenyl; and
 further provided that R^1 is not methylsulfonylphenyl;
 or
 275 a pharmaceutically-acceptable salt or tautomer
 thereof.

130. A compound of Formula IA

1187

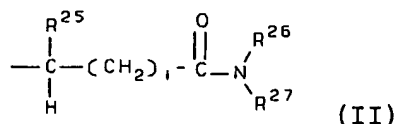


wherein

- 5 R^1 is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxycarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxycarbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene, arylcarbonyloxyarylene, and heterocyclylcarbonyloxyarylene; or

R^1 has the formula

1188



wherein:

```
35      i is an integer from 0 to 9;
```

R²⁵ is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene; and

R²⁶ is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxy carbonylalkylene, and alkylaminoalkyl; and

R²⁷ is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, alkylaryloxy carbonylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, alkoxycarbonylheterocyclylarylene, alkoxycarbonylalkoxylarylene, heterocyclylcarbonylalkylarylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene,

1189

aralkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, arylsulfonylaminoalkylene,
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,
70 heterocyclylalkylene, alkylheterocyclylarylene,
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
aryloxycarbonylarylene, arylcarbonylarylene,
alkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, and alkylsulfonylarylene groups
75 may be optionally substituted with one or more radicals
independently selected from alkyl, halo, haloalkyl,
alkoxy, keto, amino, nitro, and cyano; or

R^{27} is $-CHR^{28}R^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
is selected from aralkyl, aralkoxyalkylene,
80 heterocyclylalkylene, alkylheterocyclylalkylene,
alkoxycarbonylalkylene, alkylthioalkylene, and
aralkylthioalkylene; wherein said aralkyl and
heterocyclyl groups may be optionally substituted with
one or more radicals independently selected from alkyl
85 and nitro; or

R^{26} and R^{27} together with the nitrogen atom to which
they are attached form a heterocycle, wherein said
heterocycle is optionally substituted with one or more
radicals independently selected from alkyl, aryl,
90 heterocyclyl, heterocyclylalkylene,
alkylheterocyclylalkylene, aryloxyalkylene,
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
alkoxycarbonylamino; wherein said aryl,
95 heterocyclylalkylene and aryloxyalkylene radicals may be
optionally substituted with one or more radicals
independently selected from halogen, alkyl and alkoxy;
and

R^2 is selected from hydrido, halogen, mercapto,
100 alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl,
hydroxyalkyl, aralkyl, alkylheterocyclyl,

1190

heterocyclylalkyl, heterocyclylheterocyclyl,
heterocyclylalkylheterocyclyl, alkylamino, alkenylamino,
alkynylamino, arylamino, aryl(hydroxyalkyl)amino,
105 heterocyclylamino, heterocyclylalkylamino, aralkylamino,
N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl,
aminoalkylamino, aminocarbonylalkylene,
arylaminoalkylene, alkylaminoalkylene, arylaminoarylene,
alkylaminoarylene, alkylaminoalkylamino,
110 alkylcarbonylaminoalkylene,
aminoalkylcarbonylaminoalkylene,
alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl,
aminoalkylthio, alkylaminocarbonylalkylthio,
alkylaminoalkylaminocarbonylalkylthio, alkoxy,
115 heterocyclyloxy, alkylthio, cyanoalkylthio, alkenylthio,
alkynylthio, carboxyalkylthio, arylthio,
heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl,
alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl,
alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl,
120 carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl,
alkoxycarbonylalkyl, alkoxycarbonylalkylamino,
alkoxycarbonylheterocyclyl,
alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,
alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,
125 alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl,
aralkylthio, heterocyclylalkylthio, aminoalkoxy,
cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,
alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; wherein
the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and
130 cycloalkenyl groups may be optionally substituted with
one or more radicals independently selected from halo,
keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl,
aralkyl, heterocyclylalkyl, epoxyalkyl,
amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy,
135 haloalkyl, alkylamino, alkynylamino,
alkylaminoalkylamino, heterocyclylalkylamino,
alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,

1191

arylsulfonyl, and aralkylsulfonyl; or

140 R^2 is R^{200} -heterocyclyl- R^{201} , R^{200} -aryl- R^{201} , or R^{200} -cycloalkyl- R^{201} wherein:

R^{200} is selected from:

- $(CR^{202}R^{203})_y-$;
- $C(O)-$;
- $C(O)-(CH_2)_y-$;
- 145 - $C(O)-O-(CH_2)_y-$;
- $(CH_2)_y-C(O)-$;
- $O-(CH_2)_y-C(O)-$;
- $NR^{202}-$;
- $NR^{202}-(CH_2)_y-$;
- 150 - $(CH_2)_y-NR^{202}-$;
- $(CH_2)_y-NR^{202}-(CH_2)_z-$;
- $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$;
- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$;
- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$;
- 155 - $S(O)_x-(CR^{202}R^{203})_y-$;
- $(CR^{202}R^{203})_y-S(O)_x-$;
- $S(O)_x-(CR^{202}R^{203})_y-O-$;
- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$;
- $O-(CH_2)_y-$;
- 160 - $(CH_2)_y-O-$;
- $S-$; and
- $O-$;

or R^{200} represents a bond;

165 R^{201} represents one or more radicals selected from the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, 170 haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,

1192

alkylamino, aralkylamino, alkylaminoalkylene,
 175 aminocarbonyl, alkylcarbonylamino,
 alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,
 alkylaminoalkylcarbonylamino,
 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,
 alkoxylalkylcarbonylamino, alkoxycarbonylaminoalkylene,
 180 alkylimidocarbonyl, amidino, alkylamidino,
 aralkylamidino, guanidino, guanidinoalkylene, and
 alkylsulfonylamino; and

R^{202} and R^{203} are independently selected from hydrido,
 alkyl, aryl and aralkyl; and

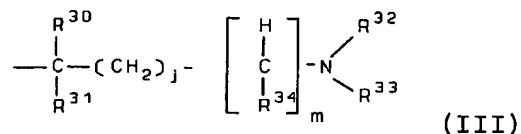
185 y and z are independently 0, 1, 2, 3, 4, 5 or 6
 wherein y + z is less than or equal to 6; and

x is 0, 1 or 2; or

R^2 is $-NHCR^{204}R^{205}$ wherein R^{204} is alkylaminoalkylene,
 and R^{205} is aryl; or

190 R^2 is $-C(NR^{206})R^{207}$ wherein R^{206} is selected from
 hydrogen and hydroxy, and R^{207} is selected from alkyl,
 aryl and aralkyl; or

R^2 has the formula:



195 wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

R^{30} and R^{31} are independently selected from hydrogen,
 alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene,
 200 aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,
 alkoxyalkyl, and alkylcarbonyloxyalkyl; and

R^{32} is selected from hydrogen, alkyl, aralkyl,
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,
 205 alkylcarbonylalkylene, arylcarbonylalkylene, and

1193

heterocyclylcarbonylaminoalkylene;

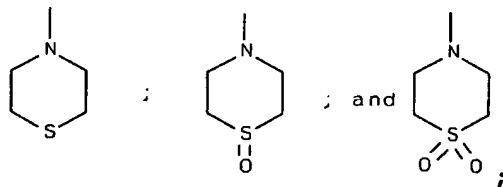
R^{33} is selected from hydrogen, alkyl, $-C(O)R^{35}$,
 $-C(O)OR^{35}$, $-SO_2R^{36}$, $-C(O)NR^{37}R^{38}$, and $-SO_2NR^{39}R^{40}$,
 wherein

210 R^{35} , R^{36} , R^{37} , R^{38} , R^{39} and R^{40} are independently
 selected from hydrocarbon, heterosubstituted hydrocarbon
 and heterocyclyl; and

R^{34} is selected from hydrogen, alkyl, aminocarbonyl,
 alkylaminocarbonyl, and arylaminocarbonyl; or

215 R^2 is $-CR^{41}R^{42}$ wherein R^{41} is aryl, and R^{42} is hydroxy;
 and

R^3 is selected from pyridinyl, pyrimidinyl,
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,
 thiazolylalkyl, thiazolylamino,

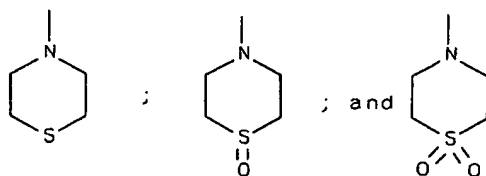


220

wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl,
 purinyl groups are substituted with one or more radicals
 independently selected from keto, haloarylamino,
 225 alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl,
 alkoxyalkylamino, alkylaminoalkoxy, alkoxyarylamino,
 alkylsulfonylamino, aryl(hydroxyalkyl)amino,
 alkylaminoalkylaminoalkylamino, alkylheterocyclylamino,
 alkylheterocyclylalkylamino,
 230 heterocyclylheterocyclylalkylamino,
 alkoxyacylheterocyclylamino and haloalkylsulfonyl;
 and

wherein the R^3 maleimidyl, pyridonyl, thiazolyl,
 thiazolylalkyl, thiazolylamino,

1194



235

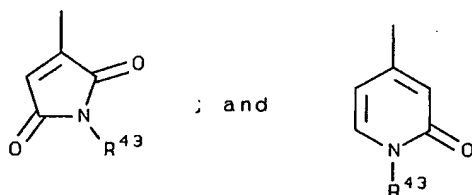
groups may be optionally substituted with one or more radicals independently selected from halo, keto, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloarylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclylloxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and -NR⁴⁴R⁴⁵ wherein R⁴⁴ is alkylcarbonyl or amino, and R⁴⁵ is alkyl or aralkyl; and

R⁴ is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R⁴ is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

265

1195

- alkylsulfinylalkylene, arylsulfinylalkylene,
 alkylsulfonyl, alkylsulfonylalkylene,
 270 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
 nitro, alkylamino, arylamino, alkylaminoalkylene,
 arylaminoalkylene, aminoalkylamino, and hydroxy;
 275 provided R^3 is not 2-pyridinyl when R^4 is a phenyl
 ring containing a 2-hydroxy substituent and when R^1 is
 hydrido; and
 provided R^3 is not



280

(IV)

(V)

wherein R^{43} is selected from hydrogen, alkyl,
 aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;
 and

285

further provided R^2 is selected from aryl,
 heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl
 when R^4 is hydrido; and

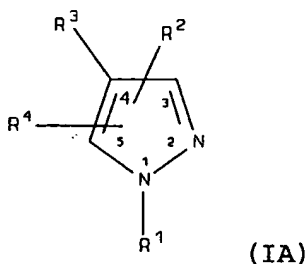
further provided that R^4 is not methylsulfonylphenyl
 or aminosulfonylphenyl; and

290

further provided that R^1 is not methylsulfonylphenyl;
 or
 a pharmaceutically-acceptable salt or tautomer
 thereof.

131. A compound of Formula IA

1196



wherein

- 5 R^1 is selected from hydroxy and alkoxyaryl; and
 R^2 is selected from hydrido, halogen, mercapto,
 alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl,
 hydroxyalkyl, aralkyl, alkylheterocyclyl,
 heterocyclylalkyl, heterocyclylheterocyclyl,
 10 heterocyclylalkylheterocyclyl, alkylamino, alkenylamino,
 alkynylamino, arylamino, aryl(hydroxyalkyl)amino,
 heterocyclylamino, heterocyclylalkylamino, aralkylamino,
 N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl,
 aminoalkylamino, aminocarbonylalkylene,
 15 arylaminoalkylene, alkylaminoalkylene, arylaminoarylene,
 alkylaminoarylene, alkylaminoalkylamino,
 alkylcarbonylaminoalkylene,
 aminoalkylcarbonylaminoalkylene,
 alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl,
 20 aminoalkylthio, alkylaminocarbonylalkylthio,
 alkylaminoalkylaminocarbonylalkylthio, alkoxy,
 heterocycloxy, alkylthio, cyanoalkylthio, alkenylthio,
 alkynylthio, carboxyalkylthio, arylthio,
 heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl,
 25 alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl,
 alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl,
 carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl,
 alkoxycarbonylalkyl, alkoxycarbonylalkylamino,
 alkoxycarbonylheterocyclyl,
 30 alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,
 alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,
 alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl,

1197

aralkythio, heterocyclylalkylthio, aminoalkoxy,
 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,
 35 alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; wherein
 the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and
 cycloalkenyl groups may be optionally substituted with
 one or more radicals independently selected from halo,
 keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl,
 40 aralkyl, heterocyclylalkyl, epoxyalkyl,
 amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy,
 haloalkyl, alkylamino, alkynylamino,
 alkylaminoalkylamino, heterocyclylalkylamino,
 alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,
 45 arylsulfonyl, and aralkylsulfonyl; or

R^2 is R^{200} -heterocyclyl- R^{201} , R^{200} -aryl- R^{201} , or R^{200} -
 cycloalkyl- R^{201} wherein:

R^{200} is selected from:

- $(CR^{202}R^{203})_y-$;
- 50 -C(O)-;
- C(O)-(CH₂)_y-;
- C(O)-O-(CH₂)_y-;
- 55 -O-(CH₂)_y-C(O)-;
- NR²⁰²-;
- NR²⁰²-(CH₂)_y-;
- 60 -NR²⁰²-(CH₂)_y-NR²⁰²-;
- (CH₂)_y-NR²⁰²-(CH₂)_z-;
- (CH₂)_y-C(O)-NR²⁰²-(CH₂)_z-;
- 65 -S(O)_x-(CR²⁰²R²⁰³)_y-;
- (CR²⁰²R²⁰³)_y-S(O)_x-;
- S(O)_x-(CR²⁰²R²⁰³)_y-O-;
- S(O)_x-(CR²⁰²R²⁰³)_y-C(O)-;
- O-(CH₂)_y-;
- (CH₂)_y-O-;
- S-; and

1198

-O-;

70 or R²⁰⁰ represents a bond;

R²⁰¹ represents one or more radicals selected from the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, alkoxy carbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl, alkylamino, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxy carbonylamino, alkoxyalkylcarbonylamino, alkoxy carbonylaminoalkylene, alkylimidocarbonyl, amidino, alkylamidino, aralkylamidino, guanidino, guanidinoalkylene, and alkylsulfonylamino; and

90 R²⁰² and R²⁰³ are independently selected from hydrido, alkyl, aryl and aralkyl; and

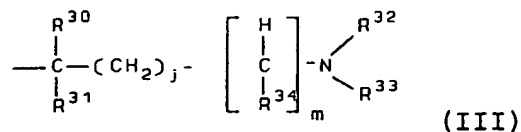
y and z are independently 0, 1, 2, 3, 4, 5 or 6 wherein y + z is less than or equal to 6; and

x is 0, 1 or 2; or

95 R² is -NHCR²⁰⁴R²⁰⁵ wherein R²⁰⁴ is alkylaminoalkylene, and R²⁰⁵ is aryl; or

R² is -C(NR²⁰⁶)R²⁰⁷ wherein R²⁰⁶ is selected from hydrogen and hydroxy, and R²⁰⁷ is selected from alkyl, aryl and aralkyl; or

100 R² has the formula:



1199

wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

105 R^{30} and R^{31} are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

110 R^{32} is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene;

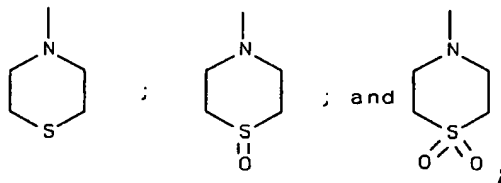
115 R^{33} is selected from hydrogen, alkyl, $-C(O)R^{35}$, $-C(O)OR^{35}$, $-SO_2R^{36}$, $-C(O)NR^{37}R^{38}$, and $-SO_2NR^{39}R^{40}$, wherein

R^{35} , R^{36} , R^{37} , R^{38} , R^{39} and R^{40} are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

120 R^{34} is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or

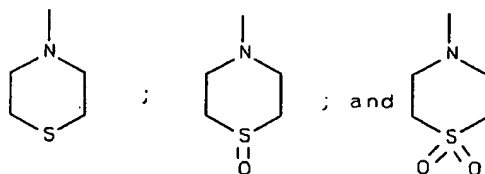
R^2 is $-CR^{41}R^{42}$ wherein R^{41} is aryl, and R^{42} is hydroxy; and

125 R^3 is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



130 wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,

1200



groups may be optionally substituted with one or more
 135 radicals independently selected from halo, keto, alkyl,
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,
 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,
 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,
 140 alkenylamino, alkynylamino, cycloalkylamino,
 cycloalkenylamino, arylamino, haloarylamino,
 heterocyclylamino, aminocarbonyl, cyano, hydroxy,
 hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,
 aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,
 145 alkoxycarbonyl, aryloxcarbonyl, heterocyclylloxycarbonyl,
 alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,
 aminosulfinyl, aminosulfonyl, alkylsulfonylamino,
 alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,
 aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,
 150 alkylheterocyclylamino, heterocyclylalkylamino,
 alkylheterocyclylalkylamino, aralkylheterocyclylamino,
 heterocyclylheterocyclylalkylamino,
 alkoxycarbonylheterocyclylamino, nitro,
 alkylaminocarbonyl, alkylcarbonylamino,
 155 haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,
 hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and -NR⁴⁴R⁴⁵
 wherein R⁴⁴ is alkylcarbonyl or amino, and R⁴⁵ is alkyl or
 aralkyl; and

R⁴ is selected from hydrido, alkyl, alkenyl, alkynyl,
 160 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein
 R⁴ is optionally substituted with one or more radicals
 independently selected from halo, alkyl, alkenyl,
 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,
 alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

1201

- 165 alkylsulfinylalkylene, arylsulfinylalkylene,
alkylsulfonyl, alkylsulfonylalkylene,
arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
170 nitro, alkylamino, arylamino, alkylaminoalkylene,
arylaminoalkylene, aminoalkylamino, and hydroxy;
provided R³ is not 2-pyridinyl when R⁴ is a phenyl
ring containing a 2-hydroxy substituent and when R¹ is
hydrido; and
175 further provided R² is selected from aryl,
heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl
when R⁴ is hydrido; and
further provided that R⁴ is not methylsulfonylphenyl
or aminosulfonylphenyl; or
180 a pharmaceutically-acceptable salt or tautomer
thereof.

132. A pharmaceutical composition comprising a
therapeutically-effective amount of a compound, said
compound selected from the compounds of any one of Claims
1, 39, 71, 82 and 94, or a pharmaceutically acceptable
5 salt thereof.

133. A method of treating a TNF mediated disorder,
said method comprising treating the subject having or
susceptible to such disorder with a therapeutically-
effective amount of a compound, said compound selected
from the compounds of any one of Claims 1, 39, 71, 82 and
5 94, or a pharmaceutically acceptable salt thereof.

134. A method of treating a p38 kinase mediated
disorder, said method comprising treating the subject
having or susceptible to such disorder with a
therapeutically-effective amount of a compound, said
compound selected from the compounds of any one of Claims

1202

5 1, 39, 71, 82 and 94, or a pharmaceutically acceptable salt thereof.

135. The method of Claim 134 wherein the p38 kinase mediated disorder is selected from the group of disorders consisting of bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid
5 arthritis, gout, psoriasis, topical inflammatory disease state, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Crohn's disease, ulcerative colitis,
10 inflammatory bowel disease and cachexia.

136. The method of Claim 134 wherein the p38 kinase mediated disorder is inflammation.

137. The method of Claim 134 wherein the p38 kinase mediated disorder is arthritis.

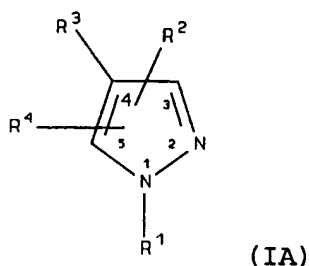
138. The method of Claim 134 wherein the p38 kinase mediated disorder is asthma.

139. A method of treating inflammation, said method comprising treating the subject having or susceptible to inflammation with a therapeutically-effective amount of a compound, said compound selected from the compounds of
5 any one of Claims 1, 39, 71, 82 and 94, or a pharmaceutically acceptable salt thereof.

140. A method of treating arthritis, said method comprising treating the subject having or susceptible to arthritis with a therapeutically-effective amount of a compound, said compound selected from the compounds of any one of Claims 1, 39, 71, 82 and 94, or a
5 pharmaceutically acceptable salt thereof.

1203

141. A method of preparing pyrazoles of Formula IA

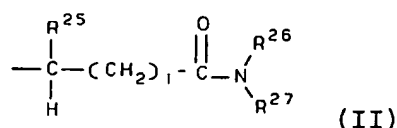


wherein

- R^1 is selected from hydrido, hydroxy, alkyl,
- 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
- 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino,
- 15 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxy carbonyl, alkoxy carbonylalkylene, aryloxy carbonylalkylene, heterocyclyloxy carbonylalkylene, alkoxy carbonylarylene, aryloxy carbonylarylene, heterocyclyloxy carbonylarylene, alkyl carbonylalkylene, aryl carbonylalkylene,
- 20 heterocyclyl carbonylalkylene, alkyl carbonylarylene, aryl carbonylarylene, heterocyclyl carbonylarylene, alkyl carbonyloxyalkylene, aryl carbonyloxyalkylene, heterocyclyl carbonyloxyalkylene, alkyl carbonyloxyarylene, aryl carbonyloxyarylene, and
- 25 heterocyclyl carbonyloxyarylene; or
- 30

1204

R¹ has the formula



wherein:

i is an integer from 0 to 9;

35 R²⁵ is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclcarbonylaminoalkylene; and

40 R²⁶ is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxyalkylene, and alkylaminoalkyl; and

R²⁷ is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocycl, aralkyl, cycloalkylalkylene, 45 cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocycl, alkylheterocyclalkylene, alkylheterocyclarylene, aralkylheterocycl, alkoxyalkylene, alkoxyarylene, 50 alkoxyaralkyl, alkoxyheterocycl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclalkylene, aryloxyalkoxyarylene, alkoxyalkoxyalkylene, alkoxyalkoxyheterocycl, alkoxyalkoxyheterocyclcarbonylalkylene, aminoalkyl, 55 alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxyalkoxyarylene, aryloxyalkoxyarylene, alkylaryloxyalkoxyarylene, 60 arylcarbonylarylene, alkylarylcarbonylarylene, alkoxyalkoxyheterocyclarylene, alkoxyalkoxyalkoxyarylene, heterocyclcarbonylalkylarylene, alkylthioalkylene,

1205

cycloalkylthioalkylene, alkylthioarylene,
65 aralkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, arylsulfonylaminoalkylene,
alkylsulfonylarylene, and alkylaminosulfonylarylene;
wherein said alkyl, cycloalkyl, aryl, heterocyclyl,
aralkyl, heterocyclylalkylene, alkylheterocyclylarylene,
70 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,
aryloxycarbonylarylene, arylcarbonylarylene,
alkylthioarylene, heterocyclylthioarylene,
arylthioalkylarylene, and alkylsulfonylarylene groups
may be optionally substituted with one or more radicals
75 independently selected from alkyl, halo, haloalkyl,
alkoxy, keto, amino, nitro, and cyano; or

R^{27} is $-CHR^{28}R^{29}$ wherein R^{28} is alkoxycarbonyl, and R^{29}
is selected from aralkyl, aralkoxyalkylene,
heterocyclylalkylene, alkylheterocyclylalkylene,
80 alkoxyalkylalkylene, alkylthioalkylene, and
aralkylthioalkylene; wherein said aralkyl and
heterocyclyl groups may be optionally substituted with
one or more radicals independently selected from alkyl
and nitro; or

85 R^{26} and R^{27} together with the nitrogen atom to which
they are attached form a heterocycle, wherein said
heterocycle is optionally substituted with one or more
radicals independently selected from alkyl, aryl,
heterocyclyl, heterocyclylalkylene,
90 alkylheterocyclylalkylene, aryloxyalkylene,
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and
alkoxycarbonylamino; wherein said aryl,
heterocyclylalkylene and aryloxyalkylene radicals may be
95 optionally substituted with one or more radicals
independently selected from halogen, alkyl and alkoxy;
and

R^2 is selected from mercapto,
aryl(hydroxyalkyl)amino, N-alkyl-N-alkynyl-amino,

1206

- 100 aminocarbonylalkylene, alkylcarbonylaminoalkylene,
 aminoalkylcarbonylaminoalkylene,
 alkylaminoalkylcarbonylamino, aminoalkylthio,
 alkylaminocarbonylalkylthio,
 alkylaminoalkylaminocarbonylalkylthio, cyanoalkylthio,
 105 alkenylthio, alkynylthio, carboxyalkylthio,
 alkoxycarbonylalkylthio, alkylsulfinyl, alkylsulfonyl,
 alkoxyalkyl, alkoxyalkylthio, alkoxycarbonylalkylamino,
 alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,
 aralkylthio, heterocyclylalkylthio, aminoalkoxy,
 110 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,
 alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; or
 R^2 is R^{200} -heterocyclyl- R^{201} , R^{200} -aryl- R^{201} , or R^{200} -
 cycloalkyl- R^{201} wherein:
 R^{200} is selected from:
- 115 - $(CR^{202}R^{203})_y-$;
 -C(O)-;
 -C(O)-(CH₂)_y-;
 -C(O)-O-(CH₂)_y-;
 -(CH₂)_y-C(O)-;
 120 -O-(CH₂)_y-C(O)-;
 -NR²⁰²-;
 -NR²⁰²-(CH₂)_y-;
 -(CH₂)_y-NR²⁰²-;
 -(CH₂)_y-NR²⁰²-(CH₂)_z-;
 125 -(CH₂)_y-C(O)-NR²⁰²-(CH₂)_z-;
 -(CH₂)_y-NR²⁰²-C(O)-(CH₂)_z-;
 -(CH₂)_y-NR²⁰²-C(O)-NR²⁰³-(CH₂)_z-;
 -S(O)_x-(CR²⁰²R²⁰³)_y-;
 -(CR²⁰²R²⁰³)_y-S(O)_x-;
 130 -S(O)_x-(CR²⁰²R²⁰³)_y-O-;
 -S(O)_x-(CR²⁰²R²⁰³)_y-C(O)-;
 -O-(CH₂)_y-;
 -(CH₂)_y-O-;
 -S-; and
 135 -O-;

1207

or R^{200} represents a bond;

R^{201} represents one or more radicals selected from the group consisting of hydroxy, hydroxyalkyl, cycloalkyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxyalkylene, alkoxyarylene, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclalkylcarbonyl, alkylsulfonylalkylene, aminoalkyl, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene, alkylimidocarbonyl, amidino, alkylamidino, aralkylamidino, guanidino, guanidinoalkylene, and alkylsulfonylamino; and

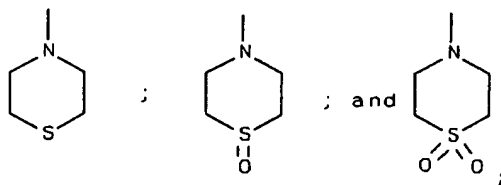
R^{202} and R^{203} are independently selected from hydrido, alkyl, aryl and aralkyl; and

y and z are independently 0, 1, 2, 3, 4, 5 or 6 wherein y + z is less than or equal to 6; and x is 0, 1 or 2; or

R^2 is $-NHCR^{204}R^{205}$ wherein R^{204} is alkylaminoalkylene, and R^{205} is aryl; or

R^2 is $-C(NR^{206})R^{207}$ wherein R^{206} is selected from hydrogen and hydroxy, and R^{207} is selected from alkyl, aryl and aralkyl; and

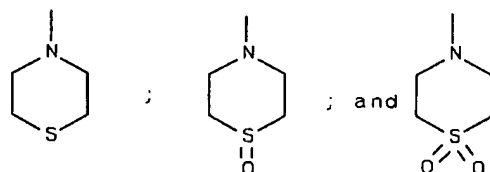
R^3 is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



wherein the R^3 pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,

1208

thiazolylalkyl, thiazolylamino,



170

groups may be optionally substituted with one or more radicals independently selected from halo, keto, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloarylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclylloxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$ wherein R^{44} is alkylcarbonyl or amino, and R^{45} is alkyl or aralkyl; and

R^4 is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R^4 is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio,

200

1209

alkylthioalkylene, arylthioalkylene, alkylsulfinyl,
alkylsulfinylalkylene, arylsulfinylalkylene,
alkylsulfonyl, alkylsulfonylalkylene,
205 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,
nitro, alkylamino, arylamino, alkylaminoalkylene,
arylaminoalkylene, aminoalkylamino, and hydroxy; or
210 a pharmaceutically-acceptable salt or tautomer
thereof,

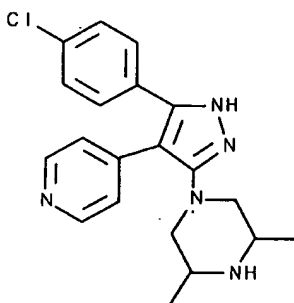
said method comprising the steps of treating a
substituted ketone with an acyl hydrazide to give the
pyrazole.

142. The process of Claim 141 wherein the process is
carried out in an acidic solvent.

143. The process of Claim 141 wherein the acidic
solvent is acetic acid.

144. The process of Claim 141 wherein the acidic
solvent is an organic solvent containing an acid.

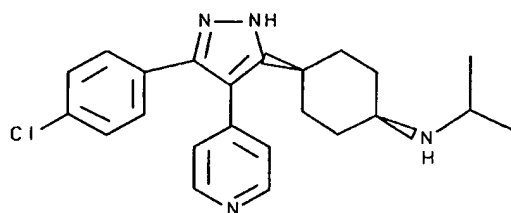
145. The compound:



or a tautomer or pharmaceutically acceptable salt thereof.

1210

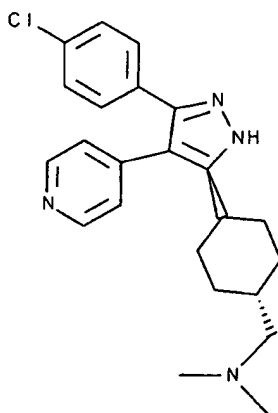
146. A compound of Claim 71 that is:



5

or a tautomer or pharmaceutically acceptable salt thereof.

147. A compound of Claim 39 that is:

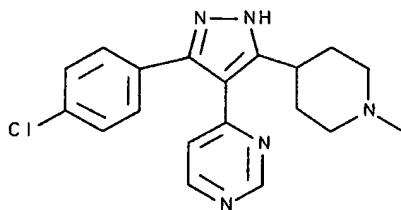


10

or a tautomer or pharmaceutically acceptable salt thereof.

148. The compound:

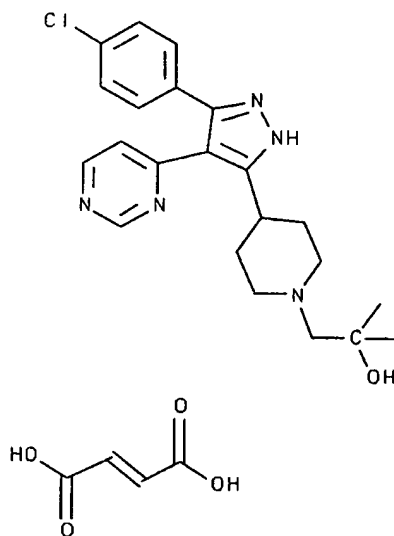
1211



15

or a tautomer or pharmaceutically acceptable salt thereof.

149. A compound of Claim 1 that is:



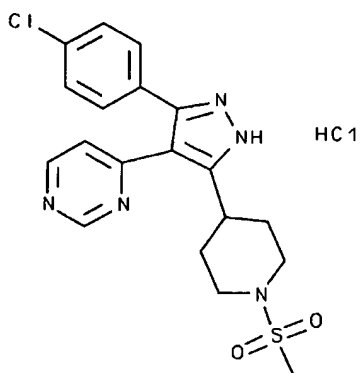
20

or a tautomer or pharmaceutically acceptable salt thereof.

25

150. The compound:

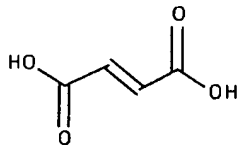
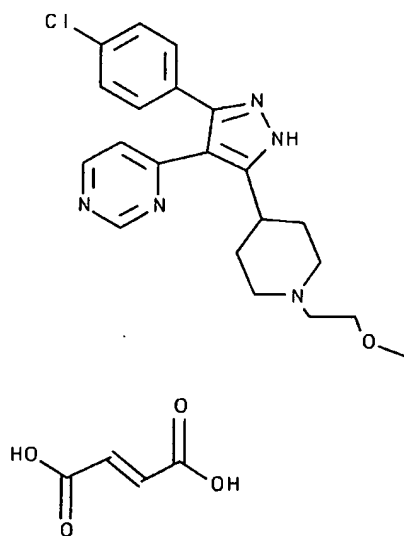
1212



or a tautomer or pharmaceutically acceptable salt thereof.

30

151. A compound of Claim 1 that is:

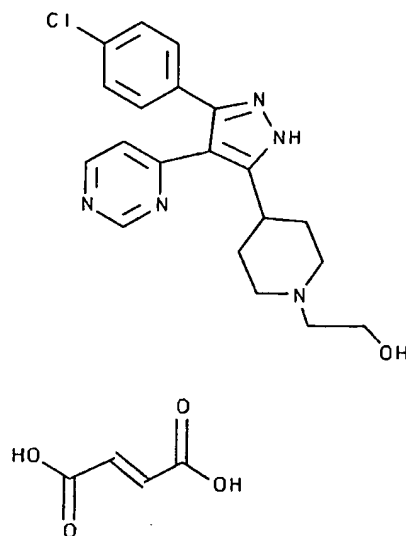


1213

or a tautomer or pharmaceutically acceptable salt thereof.

35

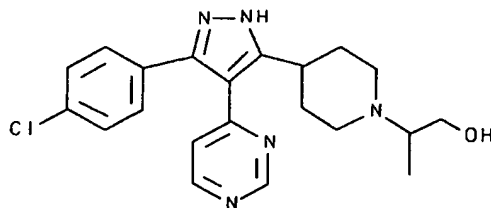
152. A compound of Claim 1 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

40

153. A compound of Claim 1 that is:

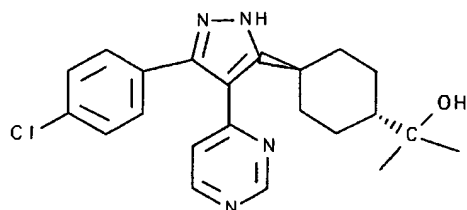


1214

or a tautomer or pharmaceutically acceptable salt thereof.

45

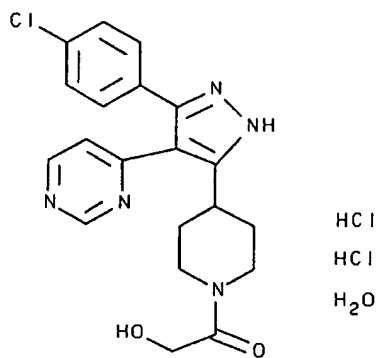
154. A compound of Claim 39 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

50

155. A compound of Claim 1 that is:

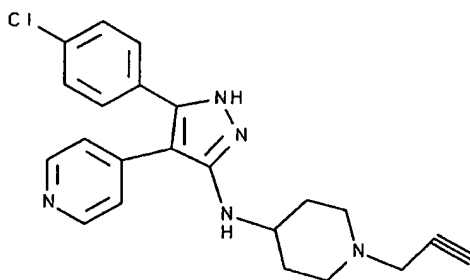


or a tautomer or pharmaceutically acceptable salt thereof.

55

156. A compound of Claim 82 that is:

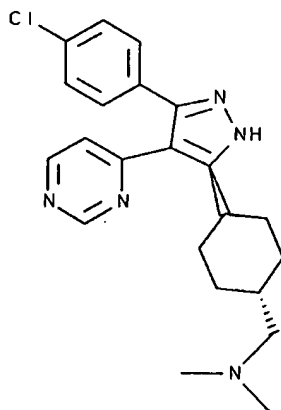
1215



or a tautomer or pharmaceutically acceptable salt thereof.

60

157. A compound of Claim 42 that is:

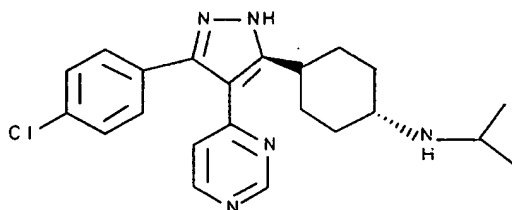


or a tautomer or pharmaceutically acceptable salt thereof.

65

158. A compound of Claim 71 that is:

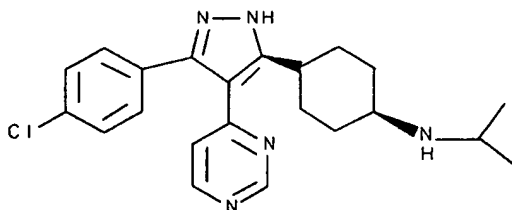
1216



or a tautomer or pharmaceutically acceptable salt thereof.

70

159. A compound of Claim 71 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

75

160. A compound of Claim 70 wherein R^{104a} is meta-chloro or para-chloro.